Gene expression in rat liver as a representative model for human aging

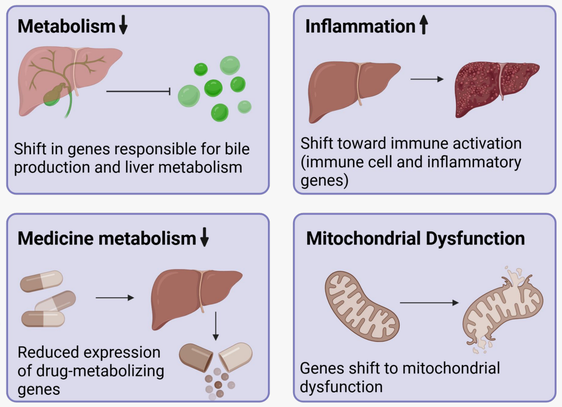
Data Science in Biomedicine – 10 October 2025 – Group 1

university of groningen

Introduction

To study drug metabolism, model organisms are needed representing the human liver. With aging, gene expression in the liver changes over time (Thomas et al., 2002).
Liver aging is partly explained by changes in the genome and epigenome, responsible for cellular senescence and low-grade inflammation. This causes multiple phenotypic changes in all liver cells (Hunt et al., 2019).
To investigate if the liver of rats represents the human liver during aging, this case study aims to compare the change in gene expression over time.

Hypothesis:



Research question

How does gene expression during aging in the rat liver represent aging of the human liver?

Methods

- Gene expression data of rat liver by Yu et al. (2014) and human liver GTEx
- Data of rats (21w and 104w)
- Data of 86 humans (20–29y and 60–69y)
- Analysis using R and R studio

Conclusion + Implication

Significantly differentiated genes for human and rat liver show to be different. Our results show that the gene expression in the liver of rats does not represent the expression in the human liver.

When comparing the results of humans with the rats: the heat map shows similar patterns of changes in gene expression. However, the similarities are not significant and in different type of genes. This could be due to the dataset or the analysis itself.

Rat models are often used to gain insights into aging when looking at the liver. Yet, species-specific differences make it crucial to carefully contextualize before applying rat data to human liver aging as shown in our results.

However, more data would be needed to confirm these findings, since the used data did not correlate with the hypothesis.

Results

Figure 1 and 2: Up- and downregulated genes in the liver during aging in rats

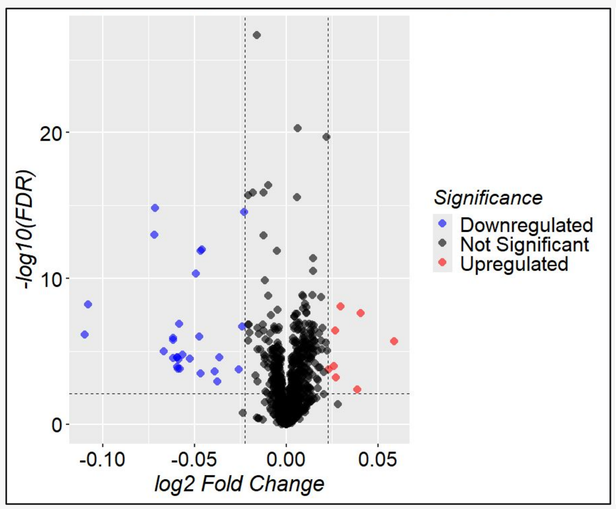


Fig. 1. Mostly downregulation of genes with increased age in rats.
In aging rats:
Genes related to immune activation and inflammation processes are upregulated. Genes related to (drug/fat) metabolism are downregulated

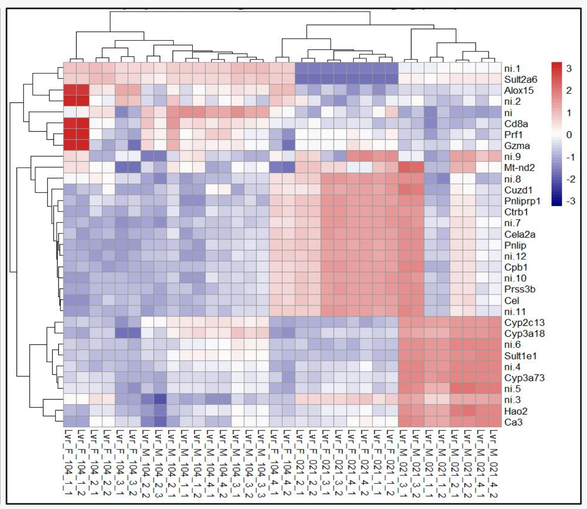


Fig. 2. Clear switch in gene expression when comparing young (right) to old (left) rats.
The majority of all genes switches from red to blue or vice versa, indicating changed expression during aging.

Figure 3 and 4: Up- and downregulated genes in the liver during aging in humans

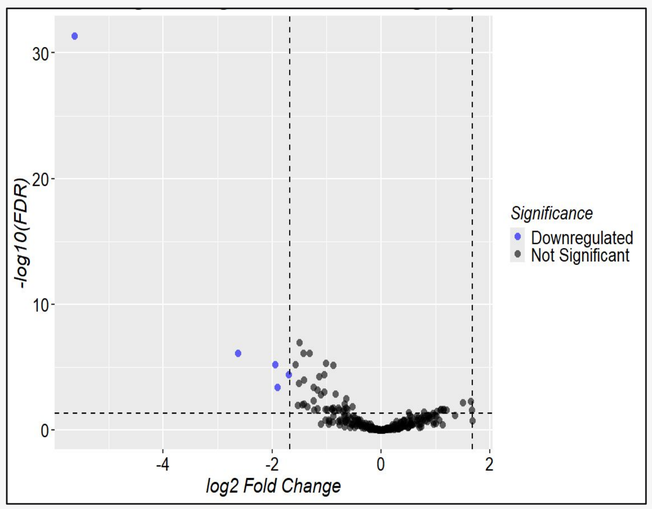


Fig. 3. Only downregulation of significant genes with increased age in humans
For humans, there is downregulation visible for a gene related to a heat shock protein, involved in ATP hydrolysis. It is activated in cellular responses against heat (NCBI, 2025). There are no significant upregulated genes for humans

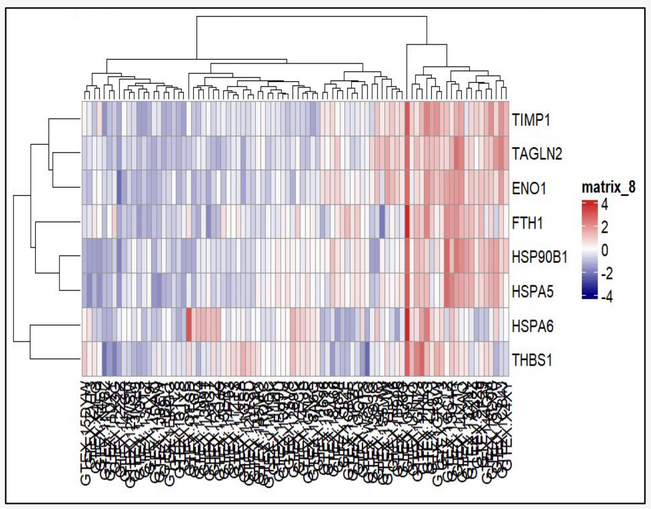


Fig. 4. Switch in gene expression when comparing young (right) to old (left) humans.
When comparing older with younger individuals, gene expression has been generally decreased. This indicates a change in gene expression during aging.

HSPA6 heat shock protein family A (Hsp70) member 6 [Homo sapiens (human)] - Gene - NCBI. (august 2025). https://www.ncbi.nlm.nih.gov/gene/3310
Thomas, R. P., Guigneaux, M., Wood, T., & Evers, B. (2002). Age-Associated Changes in Gene Expression Patterns in the Liver. Journal Of Gastrointestinal Surgery, 6(3), 445–454. https://doi.org/10.1016/s1091-255x(01)00010-5
Wang, M. (2025, 15 juli). *Why do we care about aging in liver disease?* Liver Fellow Network. https://www.aasld.org/liver-fellow-network/core-series/why-series/why-do-we-care-about-aging-liver-disease#:~:text=Aging%20leads%20to%20an%20increase%20in%20oxidative%20stress%20and%20development,alcohol%2C%20drugs%2C%20and%20toxins.
Yu, Y., Fuscoe, J. C., Zhao, C., Guo, C., Jia, M., Qing, T., Bannon, D. I., Lancashire, L., Bao, W., Du, T., Luo, H., Su, Z., Jones, W. D., Moland, C. L., Branham, W. S., Qian, F., Ning, B., Li, Y., Hong, H., . . . Wang, C. (2014). A rat RNA-Seq transcriptomic BodyMap across 11 organs and 4 developmental stages. Nature Communications, 5(1). https://doi.org/10.1038/ncomms4230 Hunt, N. J., Kang, S. W., Lockwood, G. P., Couteur, D. G. L., & Cogger, V. C. (2019).
Hallmarks of Aging in the Liver. *Computational And Structural Biotechnology Journal*, *17*, 1151–1161. https://doi.org/10.1016/j.csbj.2019.07.021 ChatGPT for phrasing and help with coding; BioRender for generating figure.

DIFFERENTIAL GENE EXPRESSION BETWEEN THE CEREBELLUM AND PREFRONTAL CORTEX OF ALZHEIMER'S PATIENTS AND HEALTHY CONTROLS

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INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by memory loss, cognitive decline, and personality changes. AD is caused by the accumulation of amyloid-beta plaques and neurofibrillary tangles, resulting in neuronal damage and neuroinflammation, but the molecular mechanisms AD remain unclear [1, 2]. The prefrontal cortex (PFC) plays a key role in executive function and working memory. PFC connectivity is known to be detrimentally affected by AD [3]. The cerebellum, traditionally associated with motor control, is increasingly recognized for its contributions to cognition [4]. RNA-seq analysis in post-mortem brain tissue allows for differential gene expression between healthy controls and AD patients. Doing so provides greater insight into the potential molecular mechanisms that drive AD and potential therapeutic targets.

OBJECTIVE

This study aims to investigate how Alzheimer's disease differentially impacts gene expression in the prefrontal cortex and cerebellum by analysing RNA-seq data using principal component analysis (PCA) alongside a set of complementary bioinformatic and statistical tools, with the goal of identifying brain region-specific molecular signatures associated with the disease.

METHODOLOGY

We used the biostudies database for data acquisition ("Bulk RNA-seq of Postmortem Human Prefrontal Cortex and Cerebellum Brain Tissues" [5]. In R-studio we analysed the data and created the PCA and volcano plots. DESeq2 was used for differential gene expression analysis. The online tool gProfiler was used for functional gene set analysis.

PRINCIPAL COMPONENT ANALYSIS BETWEEN HEALTHY CONTROLS AND ALZHEIMER'S DISEASE PATIENTS

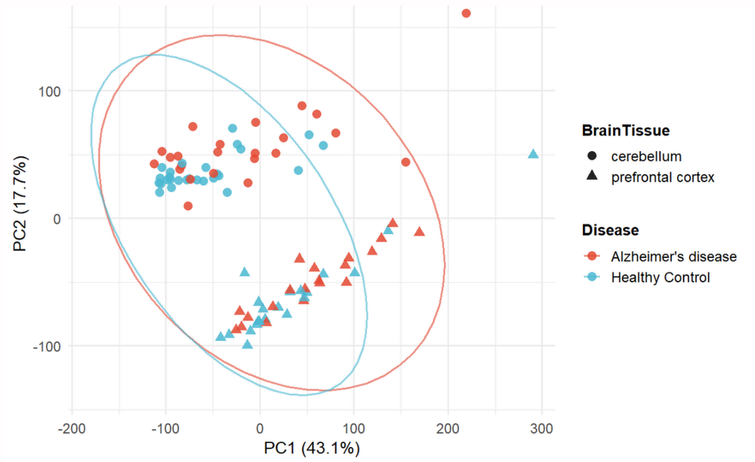


Figure 1. Principal component analysis (PCA) of RNA-seq data shows separation of Alzheimer's disease and control samples across brain regions. PCA shows distinct gene expression patterns between the cerebellum and prefrontal cortex. The first principal component explains 43.1% of the variance and the second principal component 17.7 %. Neither principal component shows a difference between healthy controls and patients.

DIFFERENTIAL GENE EXPESSION IN THE CEREBELLUM

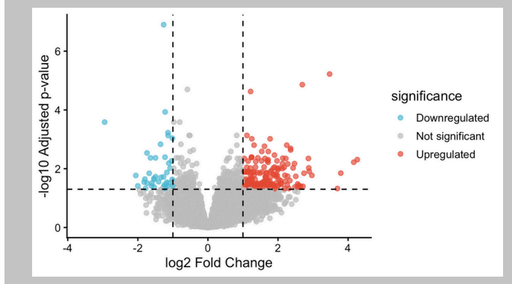


Figure 2. Volcano Plot of RNA-seq data shows significantly up- and downregulated genes in Alzheimer's disease in the cerebellum. The cerebellum of Alzheimer's disease patients shows many down- and upregulated genes *compared to controls.*

DIFFERENTIAL GENE EXPESSION IN THE PREFRONTAL CORTEX

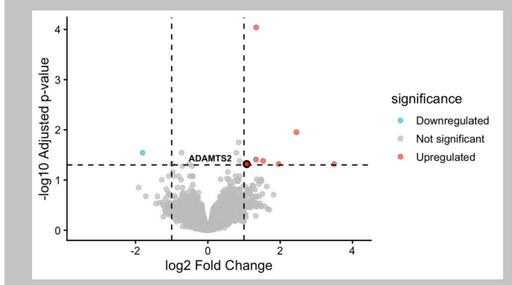


Figure 3. Volcano Plot of RNA-seq data shows limited significant up- and downregulated genes in Alzheimer's in the prefrontal cortex. The prefrontal cortex of Alzheimer's disease patients shows few down- and upregulated genes.

FUNCTIONAL GENE SET ENRICHMENT ANALYSIS

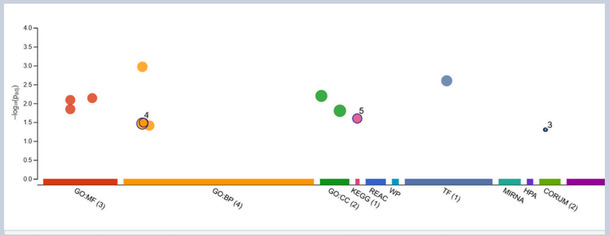


Figure 4. Functional profiling of upregulated genes in the cerebellum in Alzheimer's.

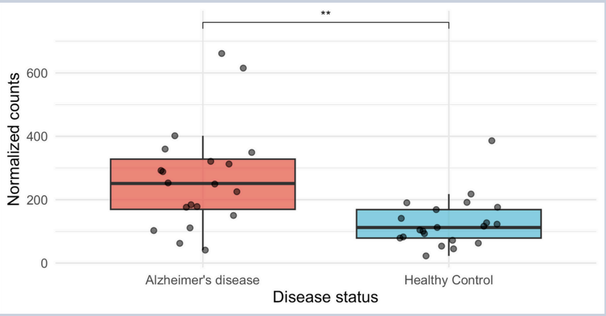


Figure 5: ADAMTS2 is upregulated in the prefrontal cortex of Alzheimer's disease patients compared to healthy controls. ** p < 0.01.

- Calcium signaling ↑ linked to synaptic dysfunction in AD [6]
- Immune receptors ↑ B-cell & cytokine complexes [7]
- Neuroinflammation ↑ defense response genes activated [7]

- ADAMTS2 expression ↑ Alzheimer's disease - role in extracellular matrix remodeling and neurodegeneration (Independent t-test: p = 0.0017) [8].

CONCLUSION

- The differential expression of genes is larger between the brain regions than between AD patients and controls.
- The cerebellum exhibits a significantly greater variation in gene expression compared to the prefrontal cortex.
- Genes related to neuroinflammation are upregulated in the cerebellum of AD patients and can therefore be potential drug targets.

SOURCES

Unraveling Sexual Dimorphism in Rat Brain Gene Expression during Early Developmental Stages

3

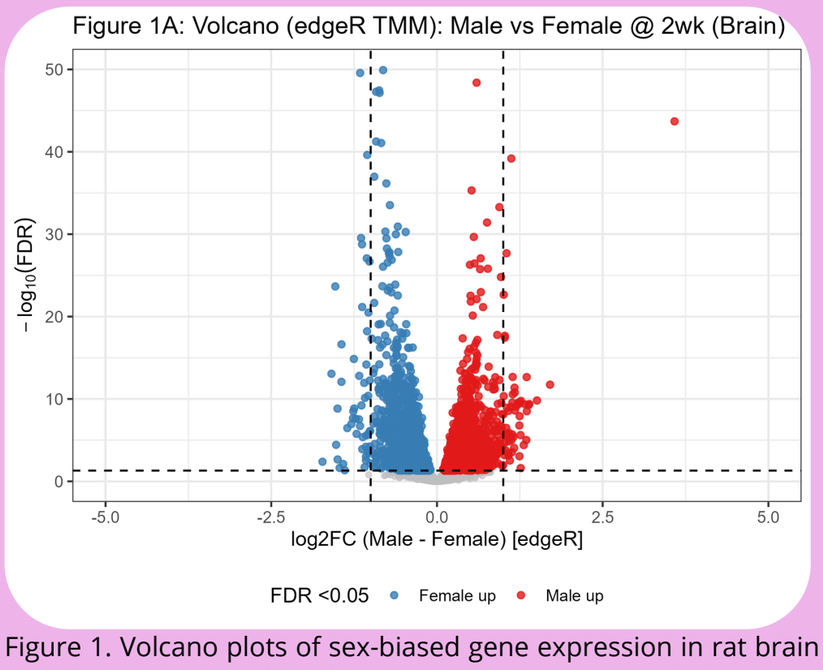
Léon Spa, Robert Dallos, Sander Uil, Sieuwert Molema, Suzanne Malikova, Thijs Neijmeijer
RUG: MSc Biomedical Sciences - Data Science in Biomedicine 10/10/2025

Introduction

Sex differences are a prominent feature of developmental brain diseases [1]. Understanding when these differences occur could shed light on the mechanisms of neurodevelopmental disorders. Furthermore, females are often excluded or overlooked in gene expression analyses. Therefore, we sought to investigate whether there are differences in gene expression between male and female rat brain development. To do this, we used RNA-seq data from Yu et al. (2014) [2]. From these data, we focused on juvenile and adolescent rats to capture early development. We hypothesized that visible sex differences in gene expression would emerge in late development, as that is when sex differences become phenotypically apparent.

Methods

We used the RNA-sequencing dataset from Yu et al. (2014), which includes 11 organ tissues at four life stages in rats, focusing here on brain tissue at the first two stages. The dataset was normalized using the TMM (Trimmed Mean of M-values) method in edgeR. Genes with fewer than two samples showing counts greater than 1 CPM were excluded. The remaining read counts were transformed into $\log_2$ values for easier interpretation. To assess sex differences in gene expression, we generated two volcano plots comparing male and female rats at 2 and 6 weeks of age, and summarized the number of significant genes in a bar plot. To further explore the data, two PCA plots were generated to visualize differences between male and female subgroups at 2 and 6 weeks, and a heatmap to show expression patterns of sex-biased genes in the brain across these two stages.



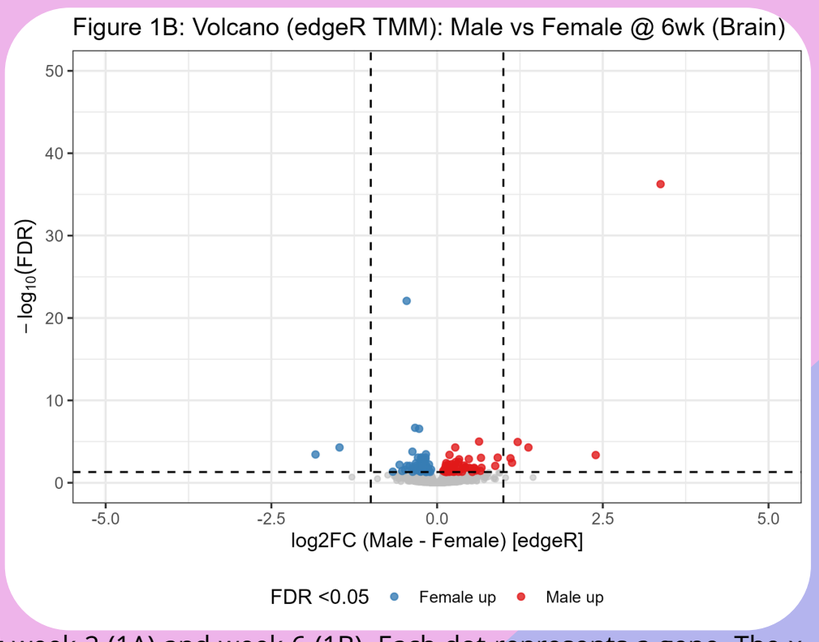


Figure 1. Volcano plots of sex-biased gene expression in rat brain at week 2 (1A) and week 6 (1B). Each dot represents a gene. The x-axis shows the $\log_2$ fold-change (Male − Female), and the y-axis shows the $-\log_{10}$ FDR (false discovery rate–adjusted p-value) from differential expression testing. Genes with FDR < 0.05 are highlighted: red = male-biased, blue = female-biased, grey = not significant. Dashed lines indicate common cutoffs (vertical: ±1 $\log_2$FC; horizontal: FDR = 0.05).

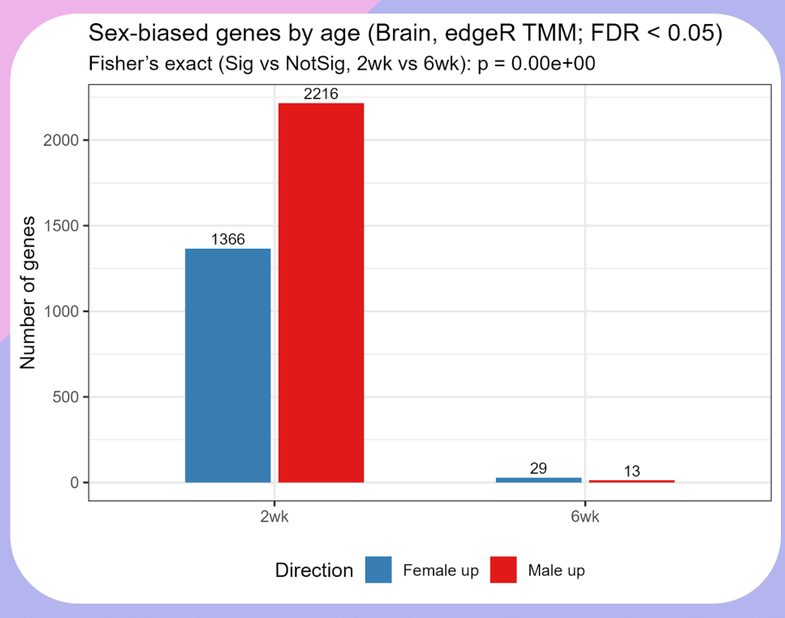


Figure 2. Numbers of sex-biased genes in rat brain at 2 and 6 weeks. Bars show counts of significantly sex-biased genes (FDR < 0.05, edgeR TMM). Red = male-biased, blue = female-biased. At 2 weeks, thousands of genes show sex-biased expression, whereas by 6 weeks only a few dozen remain. The difference in proportions of significant genes is highly significant (Fisher's exact test, $p < 1\times10^{-16}$).

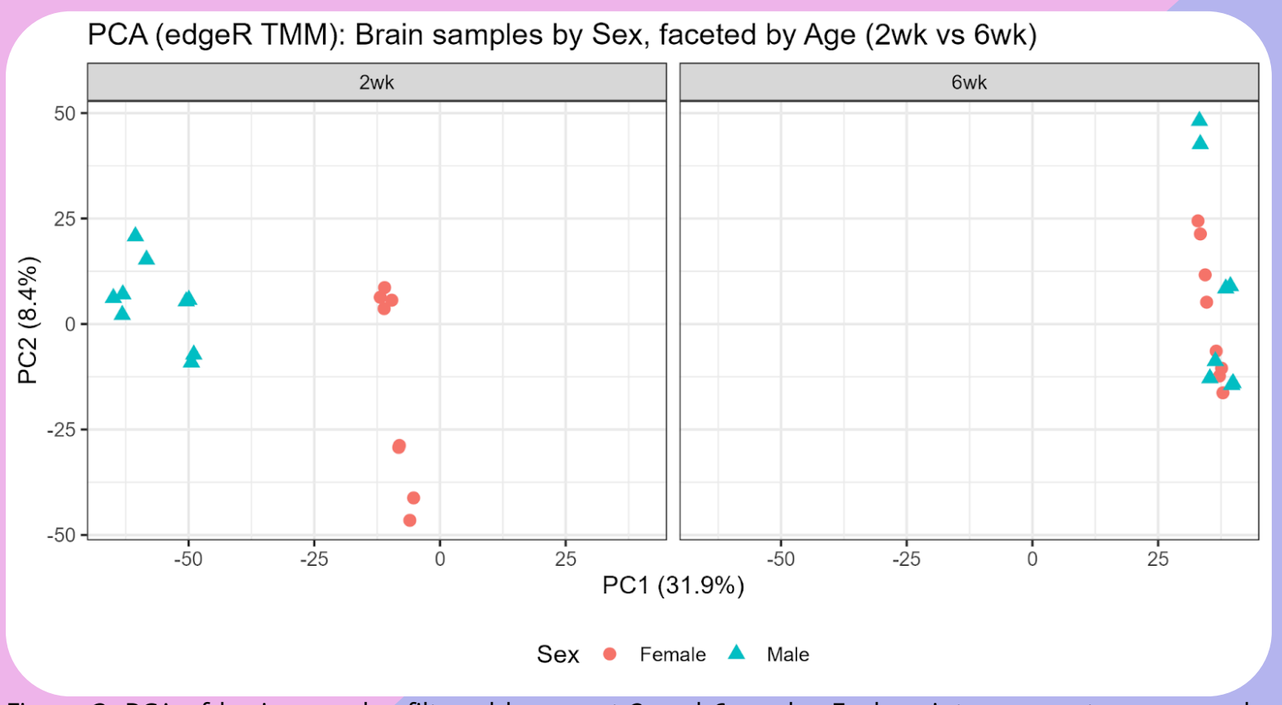


Figure 3. PCA of brain samples filtered by sex at 2 and 6 weeks. Each point represents one sample, positioned according to the first two principal components of variance in gene expression (edgeR TMM logCPM). Colors and shapes indicate sex. Panels are faceted by age group. At 2 weeks, males and females show partial separation, while by 6 weeks the separation is less pronounced, consistent with the reduction in sex-biased genes observed in differential expression analyses.

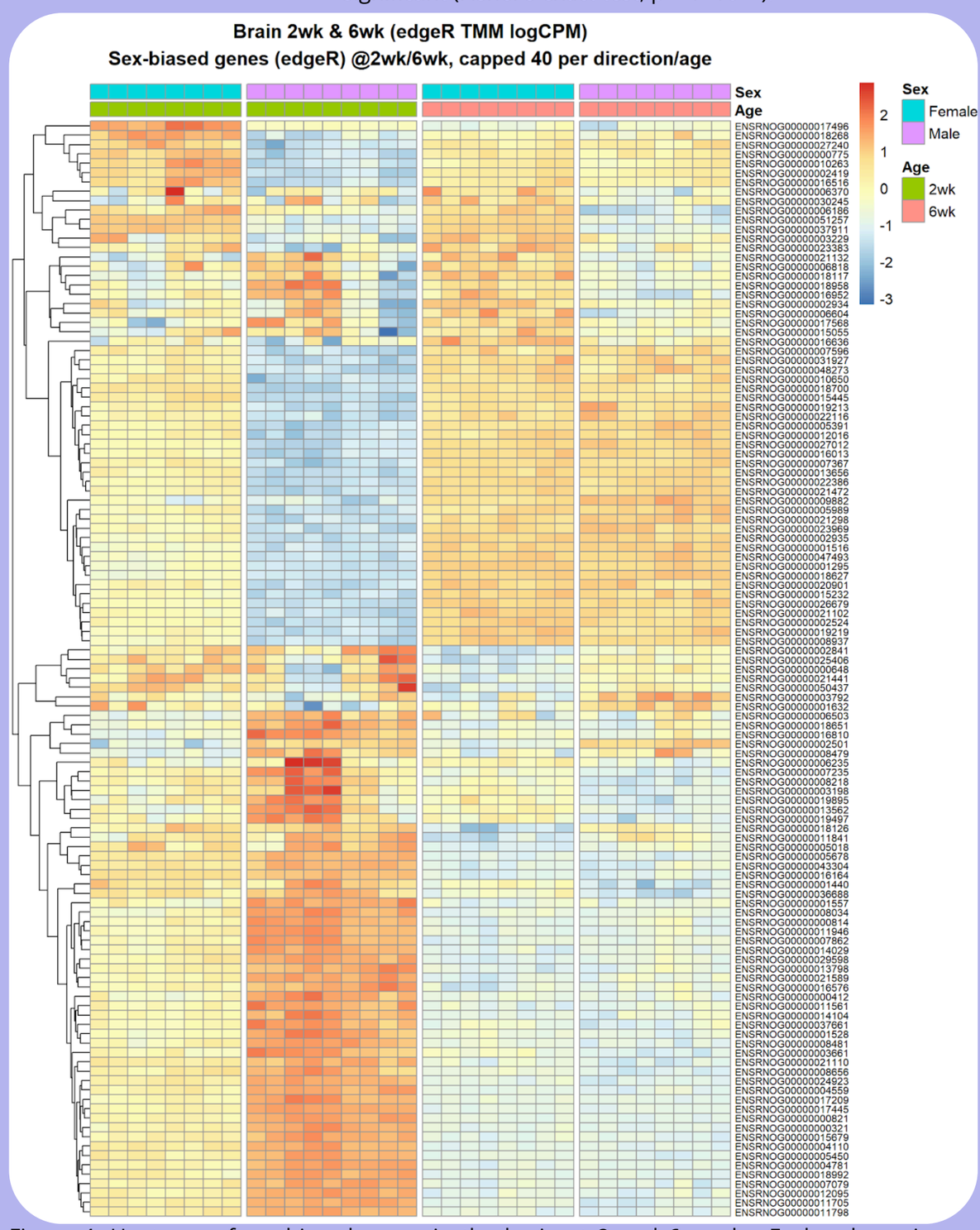


Figure 4. Heatmap of sex-biased genes in the brain at 2 and 6 weeks. Each column is one sample, annotated by Age (2 wk vs 6 wk) and Sex (Male vs Female). Rows are selected sex-biased genes (edgeR TMM, FDR < 0.05). Colors represent relative expression (z-scored per gene). Clear male–female separation is visible at 2 weeks, but weaker at 6 weeks, consistent with reduced sex-biased expression over development.

Discussion

There is a greater sex difference in brain tissue gene expression in 2-week-old rats than in 6-week-old rats. This finding was unexpected, as it contrasts with our original hypothesis. One possible explanation is the surge of testosterone in newborn male rats [3], which directly alters gene expression during early postnatal development. Although male and female brains eventually diverge phenotypically, the transcriptional differences appear to diminish once testosterone levels return to baseline, when female-typical programs are no longer suppressed [4]. These results highlight the importance of considering developmental stage in the design of drugs targeting the brain. Future studies could examine how fluctuating testosterone levels influence gene expression in the developing brain. Furthermore, studies may focus on gene ontology and translate this into human orthologs, furthering understanding of human brain development.



References, R-Code and Supplementary data :

The Influence of **Pack Years** on **COPD Genetics**

Authors Elvira Veenstra, Laura Pet, Romée Heeres, Sterre Metz, Frederick Steen, Isolde Breed

University of Groningen 10/10/25

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung disorder characterized by airflow limitation and chronic inflammation (Cosio et al., 2009; Vestbo et al., 2013) . Smoking is the primary risk factor, but the severity and progression of COPD vary widely among individuals. Cumulative smoking exposure, often measured in pack-years, may influence molecular and genetic changes in the lungs, affecting which genes are dysregulated in COPD. **Therefore, this study examines whether the extent of smoking exposure modulates the genes most strongly associated with the disease**.

Methodology

The gene expression between patients with COPD and controls (smokers without COPD) was compared for light smokers and heavy smokers . Light smokers were defined by 1 to 20 packyears (smoking one pack per day for one year) and heavy smokers by more than 20 packyears (Mahmoudinezhad et al., 2022).

Step 1 → **Step 2** → **Step 3** → **Step 4**

Data Import (RStudio)	**Format and Filter**	**DESeq2 Analysis**	**Data Visualization**
Load Kim et al. (2025) COPD data	Applying filter for 1-20 and >20 packyears	Differential expression by packyear groups	Volcano, PCA, and Scatter plots

Results

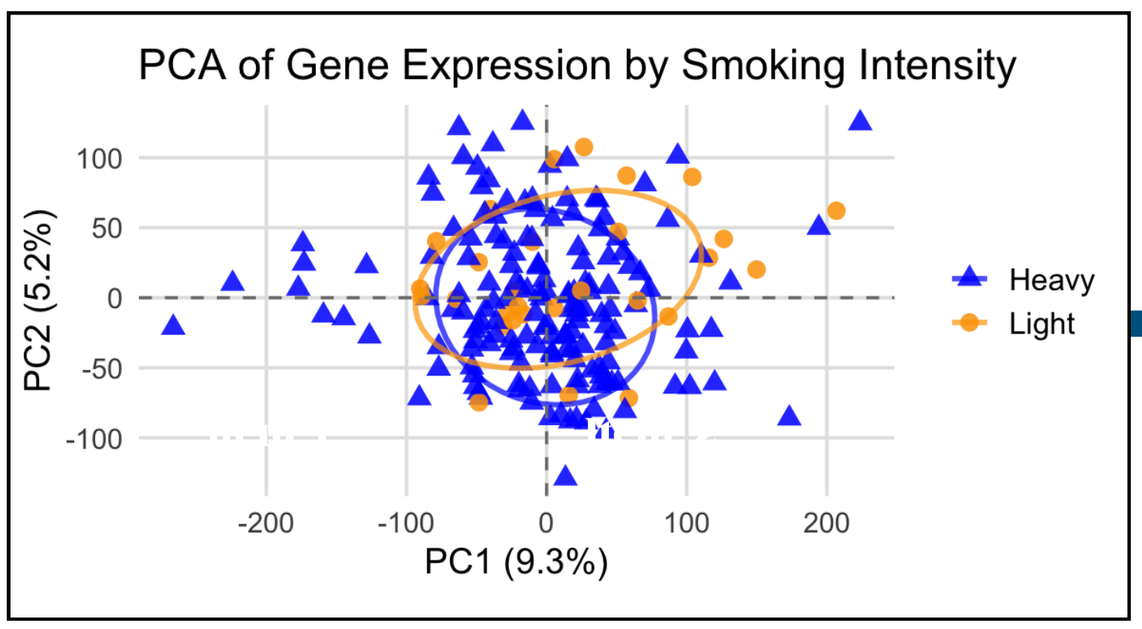


Figure 1. PCA plot showing the variation in gene expression between heavy (blue) and light (orange) smokers. The plot does not show clear clustering of the two different groups, indicating that the difference in gene expression between the two groups may not be big.

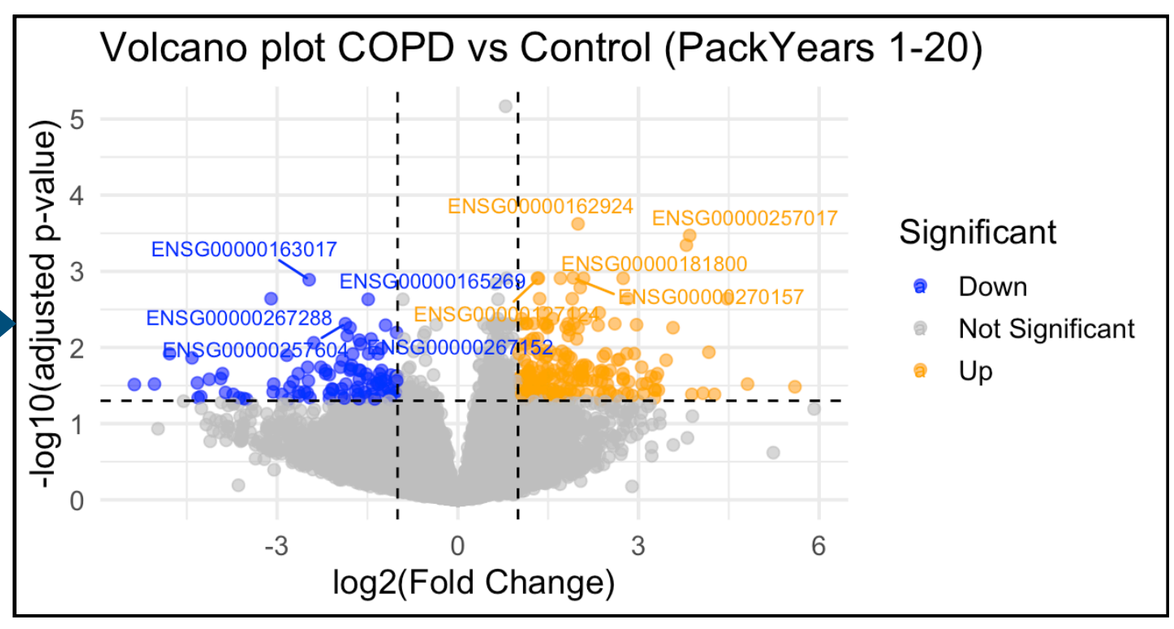


Figure 2. Volcano plot showing differential gene expression in COPD patients compared to control subjects with a smoking history of 1–20 pack-years. The 5 most significant genes that were upregulated are labeled, as well as those that were downregulated.

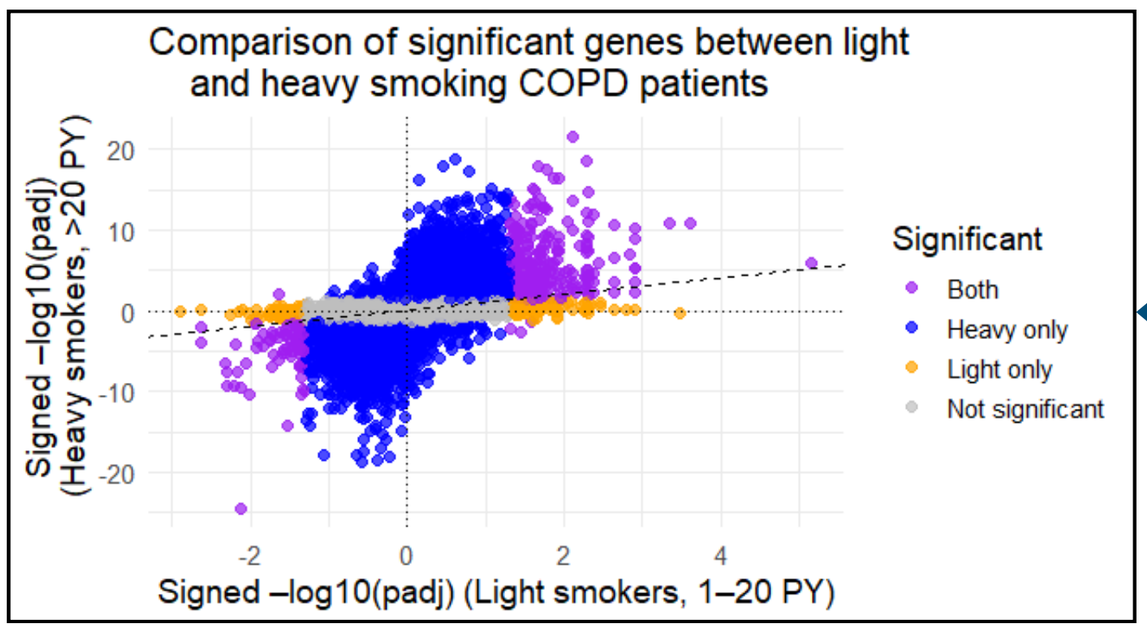


Figure 4. Scatterplot showing the signed -log10 (adjusted p-values) for differential gene expression in heavy vs light smoking COPD patients. A moderate positive correlation (r = 0.50) indicates that some genes are consistently regulated across both groups, while others are specifc to smoking intensity.

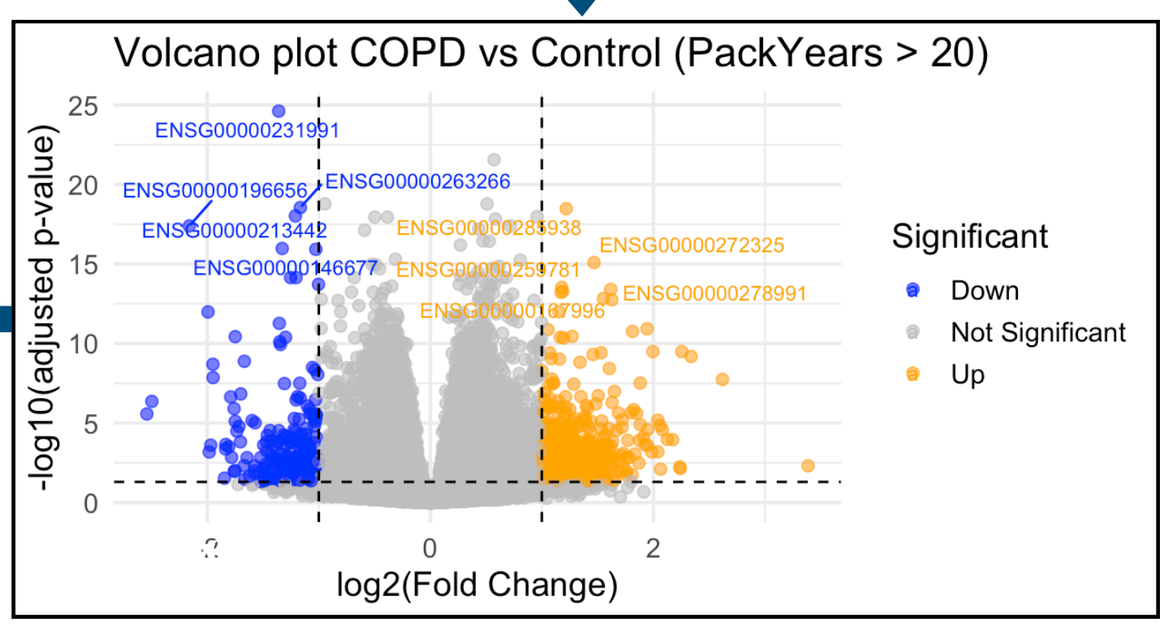


Figure 3. Volcano plot showing differential gene expression in COPD patients compared to control subjects with a smoking history of >20 pack-years. The 5 most significant genes that were upregulated are labeled, as well as those that were downregulated.

Conclusion

This study investigated whether smoking exposure, measured in pack-years, influences genes most strongly associated with COPD. DESeq2 indicated that packyears moderately affects gene expression. Comparison between light and heavy smokers revealed that the most significant genes differ between the two groups. Volcano plots suggest more COPD-associated genes in heavy smokers, but this likely reflects the larger sample size (160 vs. 28). Scatter plots show that some genes are significant in both groups, while others appear specific to heavy or light smokers. However, these observations are confounded by the unequal sample sizes. Overall, the higher number of genes significant in heavy smokers is likely influenced by sample size rather than a biological effect.

References

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How do gene expression profiles differ in COPD patients by disease severity and smoking exposure?

Annelieke Bos, Onoufrios Fragkioudakis, Robin van Nes, Rosa Rutte, Monique ter Schure, Terri Thahmaz

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a prevalent disease, causing about 3.5 million deaths worldwide in 2021 (Elflein, 2025).

The main demographic affected is smokers, as 20% of smoking individuals will eventually develop the disease (Terzikhan et al., 2016).

The disease is characterized by chronic inflammation that leads to **airway narrowing, limited airflow,** and, in advanced stages, **tissue destruction** and eventual **collapse of the respiratory system and death** (Agarwal, Raja, & Brown, 2023).

We utilized the transcriptome analyses data of lung tissues in 98 COPD patients with varied disease progression and 91 controls, as presented by Kim et al (2025), to study:

- **COPD vs Healthy controls:** identification of significantly up-/down-regulated genes in COPD patients compared to non-diseased individuals (Terri & Onoufrios)
- **COPD genes vs Grade of the disease:** Explore differential gene expressions (DGE) with increased disease progression (Annelieke & Rosa)
- **COPD genes vs Pack Year:** Assess the alteration caused by cumulative smoking (pack years) on the gene expression landscape (Robin & Monique)

RESULTS: DGE CONTROL VS COPD

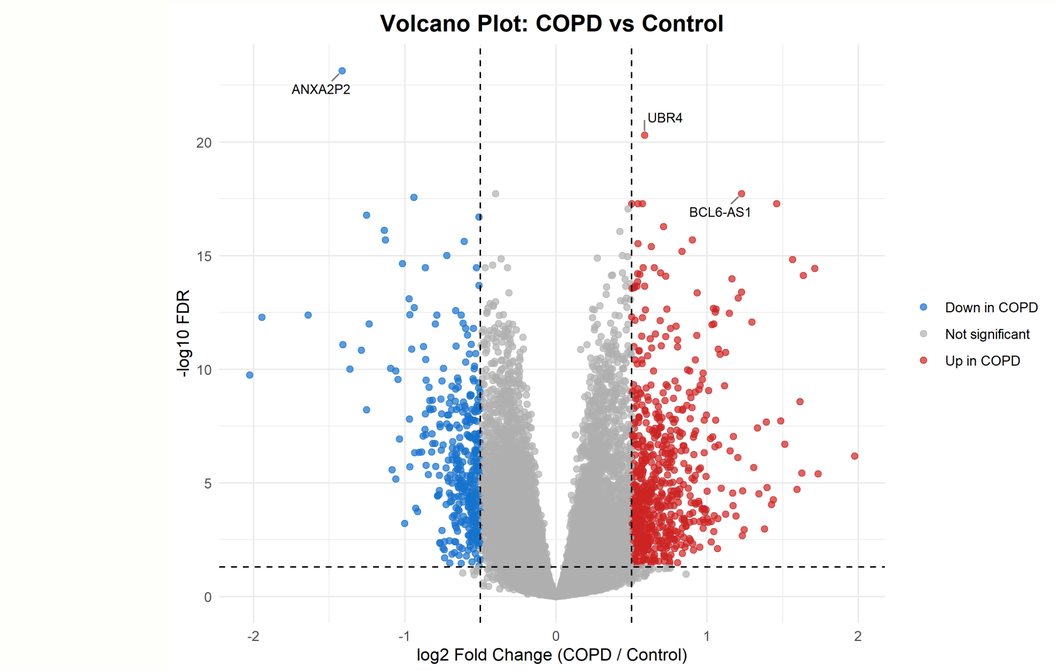


Figure 1. Differential Gene Expression Analysis of COPD Patients Compared to Healthy Controls. A volcano plot was created that displays differentially expressed genes between COPD patients and healthy controls. The Benjamini-Hochberg correction has been used due to multiple testing in addition to the quasi-likelihood F-test (glmQLFTest) that determines significance. Grey points in the plot represent genes without significant differential expression between the two groups. Red points highlight genes that are significantly upregulated in COPD, while blue points indicate genes significantly downregulated in COPD. The top three most statistically significant genes are labeled, which are **ANXA2P2, UBR4** and **BCL6-AS1.**

RESULTS: DGE MILD VS MODERATE

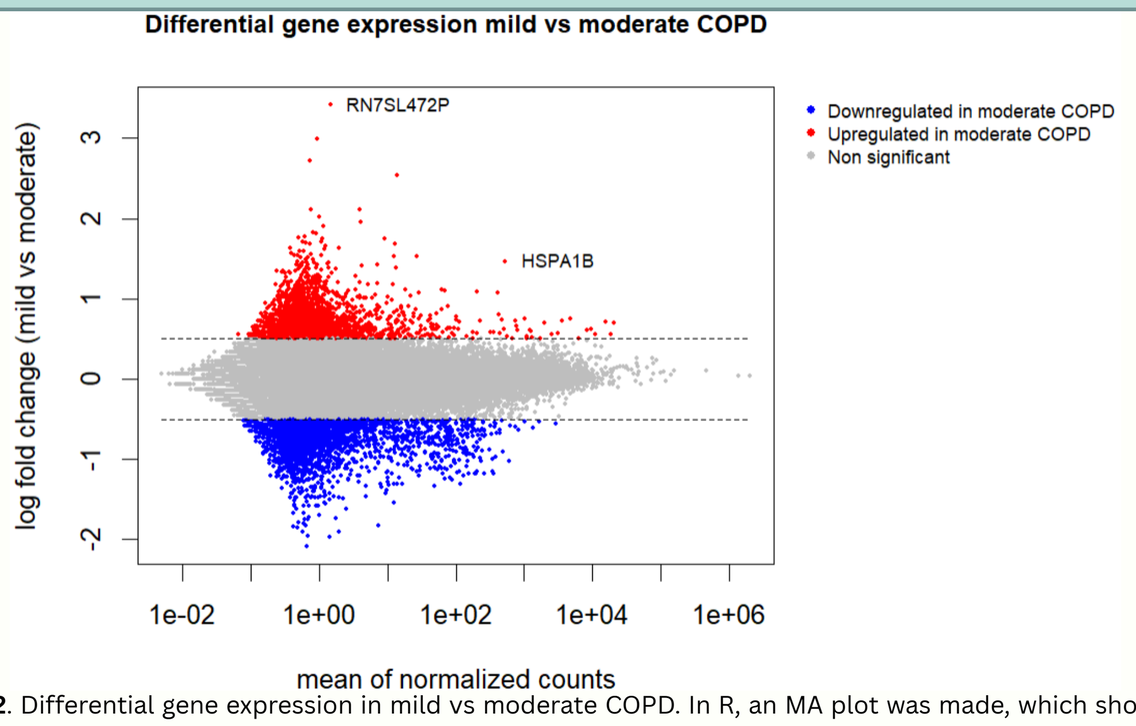


Figure 2. Differential gene expression in mild vs moderate COPD. In R, an MA plot was made, which shows the differential gene expression between mild and moderate COPD. Normalization was done with DESeq. The X-axis shows the average gene expression of the samples on a logarithmic scale. The Y-axis shows the log fold change (moderate COPD/ mild COPD). A non-significant area was added between ± 0.5 log fold change. Each dot represents a gene. The non-significant genes are grey, upregulated in moderate COPD are red, and downregulated in moderate COPD are blue. The genes with differential gene expression with a p-value < 0.05 were annotated. These are the upregulated genes **RN7SL472P** and **HSPA1B**.

RESULTS: IMPACT OF SMOKING EXPOSURE ON COPD SEVERITY AND GENE EXPRESSION

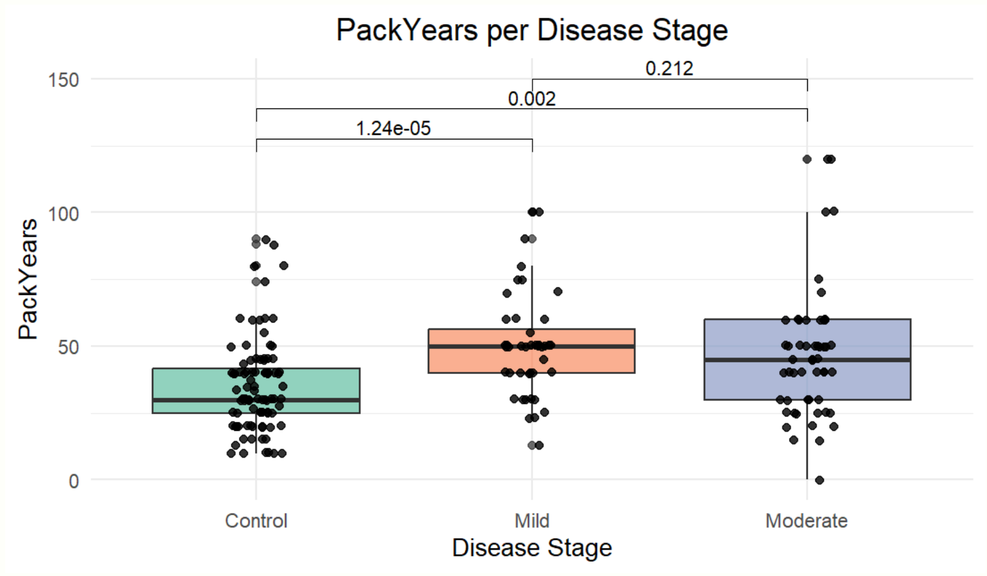


Figure 3. Distribution of smoking exposure (PackYears) across COPD disease stages (stage 0-2). The x-axis represents the stage of disease. The y-axis represents the PackYears. Black dots represent individual samples. Pairwise comparison between groups was performed using the Wilcoxon rank-sum test. Additionally, adjusted p-values (Benjamini–Hochberg correction with a threshold of $p < 0.05$) are shown. Significant differences in PackYears were observed between the control group and both Stage 1 and Stage 2 COPD, whereas no significant difference was detected between Stage 1 and Stage 2.

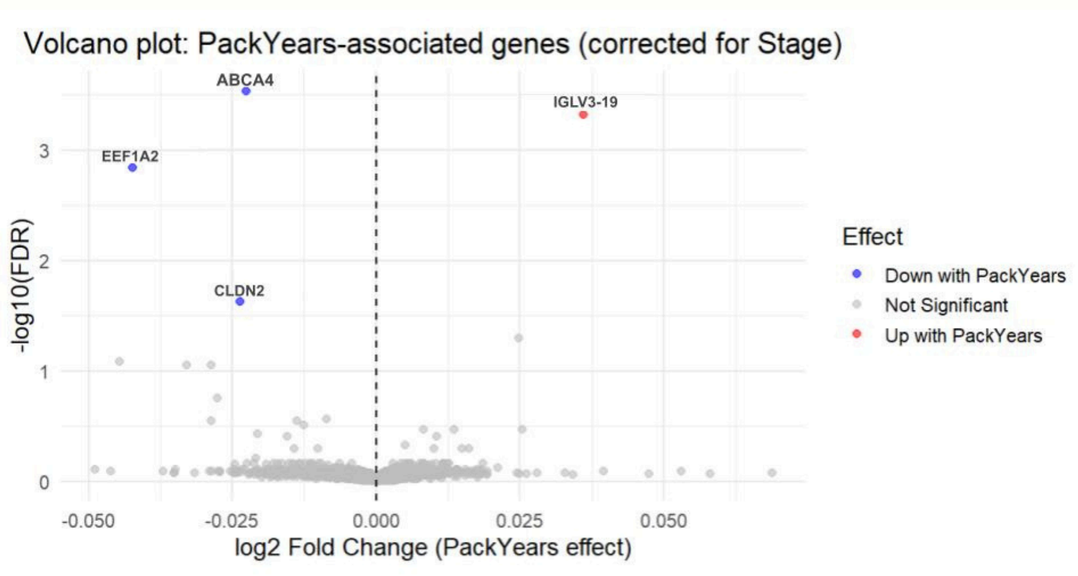


Figure 4: PackYears-associated genes, corrected for COPD disease stage. The x-axis represents the estimated $\log_2$ fold change in gene expression per unit increase in PackYears. The y-axis represents the $-\log_{10}$ of the adjusted p-value (FDR). Red dots indicate significantly upregulated genes, and blue dots indicate significantly downregulated genes (FDR < 0.05). Grey dots represent non-significant genes. Vertical dashed line denotes no change in expression ($\log_2$FC = 0).

- Gene **IGLV3-19** shows upregulation. Genes: **ABCA4**, **EEF1A2**, and **CLDN2**, show downregulation.

FUNCTIONAL OVERVIEW OF MAJOR GENES

UBR4 encodes a protein that is an E3 ubiquitin-protein ligase. It attaches to retinoblastoma-associated proteins and calcium-bound calmodulin (Dryer et al., 2025). It is also sigifnicantly expressed in COPD in the findings of Kim et al. (2025).
BCL6-AS1 is classified as a lncRNA, which is an immune regulator for T follicular cells differentiation (Dryer et al., 2025). BCL6 is regulated during hypoxia-induced pulmonary hypertension, where it increases T follicular cell activity, disrupting immunological balance (Li. et al., 2022).
HSPA1B is a heat shock protein, which are usually elevated in patients with COPD (Cappello et al., 2015).
EEF1A2 is an eukaryotic translation elongation factor found to be associated with smoke-induced COPD (Gao, 2023)
CLDN2 is a major integral membrane protein localized exclusively at tight junctions. Claudins are expressed in an organ-specific manner and regulate tissue-specific physiologic properties of tight junctions (Elkouby-Naor, 2025).
IGLV3-19 enables antigen-binding activity and is predicted to be involved in the immune response. Active smoking induced an adaptive immune response with relatively high levels of (class-switched) memory B-cells (Dryer et al., 2025).

CONCLUSION

Our DGE analysis revealed significantly expressed genes. Some of the observed genes could directly affect COPD by influencing the lung tissues, air flow, or inflammation. Others, however, could be used as biomarkers or therapeutic targets.
Smoking exposure correlates with both COPD onset and distinct gene expression changes associated with smoke-induced COPD and inflammation. Future studies should assess whether these molecular changes are reversible and if they can predict disease progression. Additionally, they should aim to reveal the exact mechanisms by which these genes affect COPD manifestation.

References

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By: Isabelle Been, Olivia Bone, Sabrina Penris, Willemijn Poelen, Sophia de Schutter, & Michelle Valderrama

Comparative Transcriptomic Analysis of Aging in Rat Brain, Liver, and Kidney



Introduction

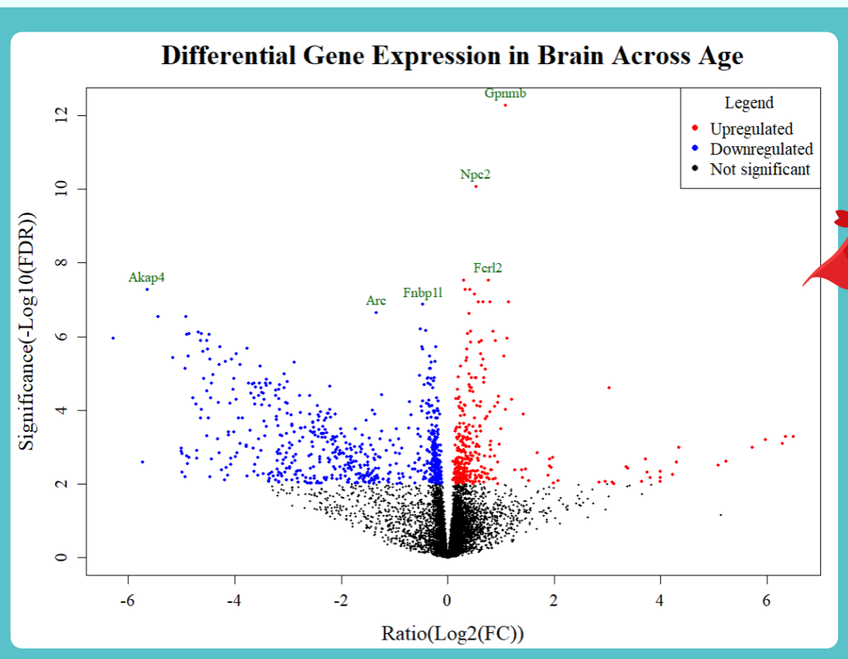
- **Yu et al. (2014)** profiled 11 rat organs across their lifespan
- We examined the **DEGs of the Brain, Liver, and Kidney between 21 weeks (adult) and 104 weeks (aged)**
- **Organ Purpose:** Kidney, brain and liver were selected because they differ in cellular composition, metabolic activity and tissue functions.
- **Age Purpose:** 21 and 104 week old rats were chosen to chosen to examine age-related changes in gene expression between young adult and older adults.
- **RQ:** How do age-related gene expression changes differ across the rat brain, liver, and kidney, and which organ shows the strongest transcriptomic signature of aging?

Methodology

1. **Data**: Gene expression in rats data from Yu et al.
2. **Filtering**: Lowly expressed genes removed using CPM thresholds
3. **Selection**: Samples filtered for the tissue of interest (brain, liver and kidneys) at age 21 and 104 weeks
4. **Analysis**: Normalization and DGA performed with edgeR
5. **Visualization**: Results placed in a volcano plot
6. **Analysis**: DEG overlap between organs shown in UpSet plot
7. Top significant genes roles identified via Ensembl.org



Volcano Plots By Organ



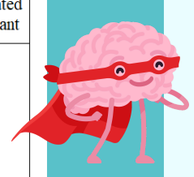


Figure 1: Volcano plot depicting differential gene expression in the Brain between 21 and 104 weeks. DGE was determined using edgeR in RStudio with the Benjamini-Hochberg FDR correction of the p-value. Each point on the graph represents a gene, with the False Discovery Rate in -Log10 on the y-axis and Fold change in Log2 on the x-axis. Significantly up and down regulated genes (FDR ≤ 0.01) are shown in red and blue, while non-significant genes are in black. The most significant genes are labeled.

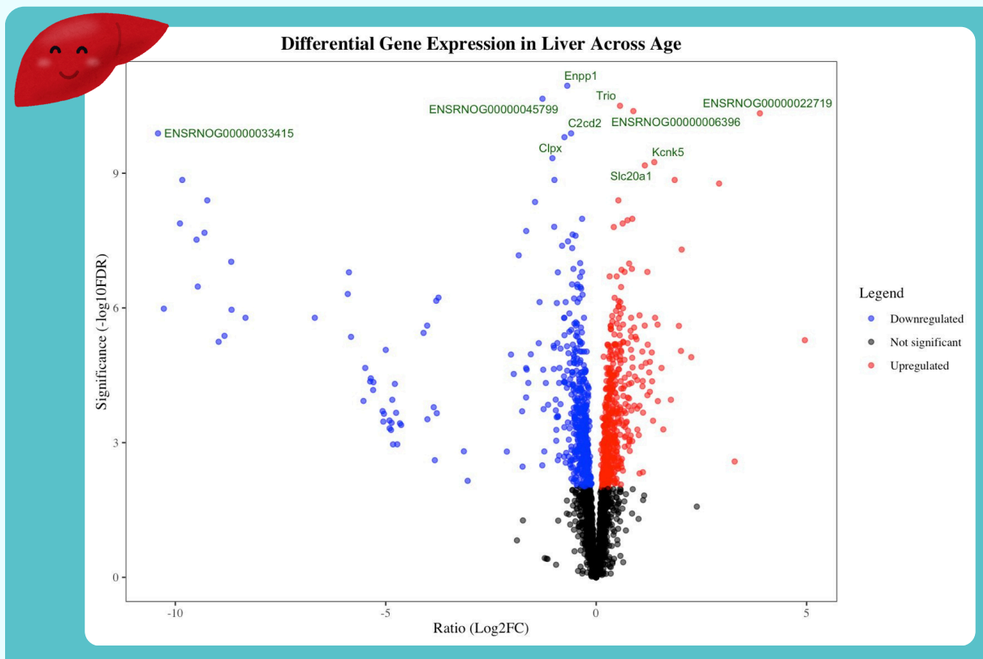


Figure 2: Volcano plot depicting differential gene expression in the Liver between 21 and 104 weeks. Axes and analysis methods are consistent with figure 1.

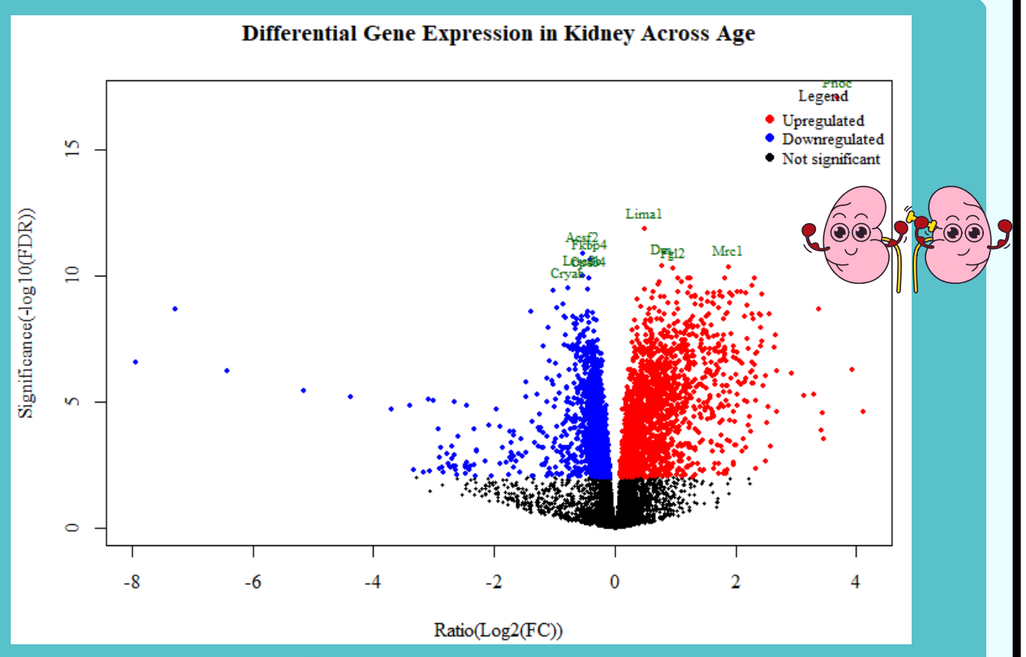


Figure 3: Volcano plot depicting differential gene expression in the Kidney between 21 and 104 weeks. Axes and analysis methods are consistent with figure 1 and 2.

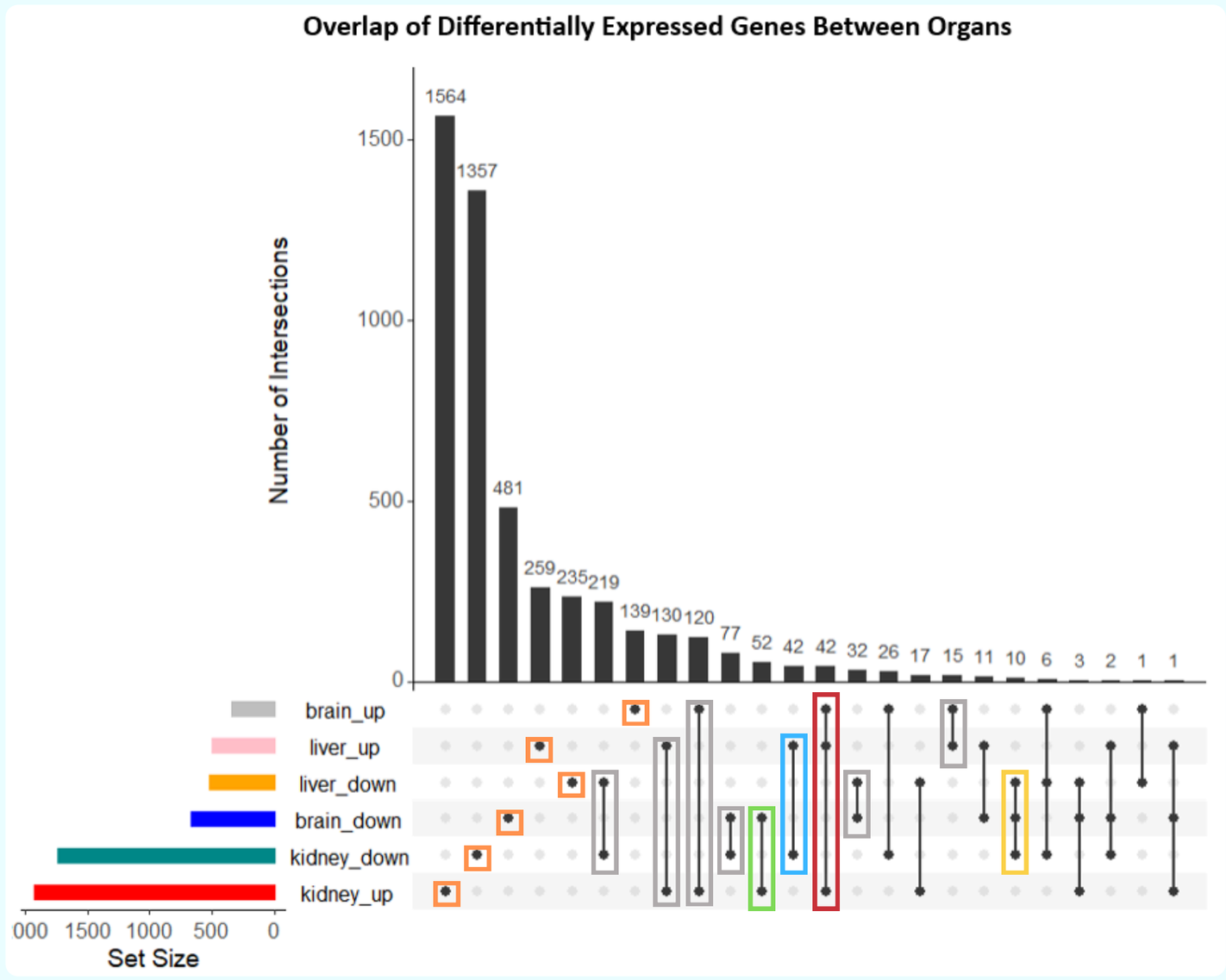


Figure 4: UpSet plot illustrating the overlap of differentially expressed genes (DEGs) across the brain, liver, and kidney between adult (21 weeks) and aged (104 weeks) rats. Set size bars (left) indicate the total number of up- or downregulated genes per organ, while intersection bars (top) show the number of genes shared across tissues. The kidney displayed the largest DEG set, indicating the strongest transcriptomic response to aging. A total of 42 genes were upregulated in all three tissues, and 10 genes were downregulated. Some intersections show opposing trends, where some genes are upregulated in one or two tissues and downregulated in another. This likely reflects tissue-specific adaptations to systemic aging signals. However, minor discrepancies could also arise from biological heterogeneity or limited sample size.

Results

- **42 genes upregulated in all tissues** (core aging genes) → Linked to systemic inflammation or immune activation.
- **10 genes downregulated in all tissues** → shared decline in metabolic function, stress resilience and cell proliferation with aging.
- **Kidney shows largest DGE count** → strongest transcriptomic response to aging.
- **Organ-specific responses** reflect age-related changes are tissue-specific, as significant DEGs in organ-specific volcano plots largely do not overlap with the core aging patterns identified in the UpSet plot.
  - Brain = Moderate alterations (mainly genes linked to neuronal signaling + synaptic function)
  - Liver = changes in metabolic + detoxification pathways
  - Kidneys = inflammation + tissue remodelling
- **Aging drives opposite gene expression across organs:**
  - Eg) Agpat 3 (lipid metabolism) can be **downregulated in kidney** due to declining metabolic and transport function, while **upregulated in the liver** as a compensatory response to maintain metabolic and protective pathways.
  - Eg) Fos/Nr4a1 (neuronal activity) can be **downregulated in the brain** due to reduced neuronal activity and cell loss, while **upregulated in the kidney** as a compensatory response to stress and metabolic demands.
- Patterns shared by **only two tissues** were often not significant in the third → focus on multi-gene overlaps to capture broader + stronger similarity patterns.

Conclusions

- Age-related gene expression changes: some shared core genes that are linked to inflammation and metabolic decline, but most changes are organ-specific.
- The kidneys exhibits the strongest transcriptomic response.
- Aging also drives opposite gene expression across different organs, reflecting tissue-specific compensatory mechanisms.

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university of groningen

TRANSCRIPTOME ANALYSIS OF LUNG TISSUES IN COPD PATIENTS
Identification of Dysregulated Genes Using RNA-Seq

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Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive lung disorder characterised by persistent airflow limitation and abnormal inflammatory responses to harmful particles or gases, most commonly cigarette smoke. It affects over 250 million people worldwide and is a leading cause of morbidity and mortality.

While inflammation, oxidative stress, and tissue remodelling are known hallmarks of COPD, the precise molecular mechanisms that drive disease progression and irreversible airflow obstruction remain incompletely understood. Conventional studies have identified some key mediators, but large-scale molecular analyses are needed to uncover global gene expression changes associated with COPD.

Transcriptome profiling using RNA sequencing (RNA-Seq) provides a powerful tool to comprehensively examine these molecular alterations. In the study by Kim et al. (2015), lung tissue RNA from 98 COPD patients and 91 controls with normal lung function was sequenced using the Illumina HiSeq 2000 platform. Their analysis identified multiple dysregulated pathways, notably those involved in oxidative phosphorylation, protein degradation, and chromatin modification, suggesting mitochondrial dysfunction and altered gene regulation in COPD lungs.

In this case study, we re-analysed the Kim et al. dataset to identify differentially expressed genes (DEGs) between COPD and control lung tissues. Our goal was to highlight the most strongly upregulated and downregulated genes and visualise expression patterns that may underlie COPD pathophysiology.

Research Question: Which genes are differentially expressed in the lung tissue of COPD patients compared to healthy controls?

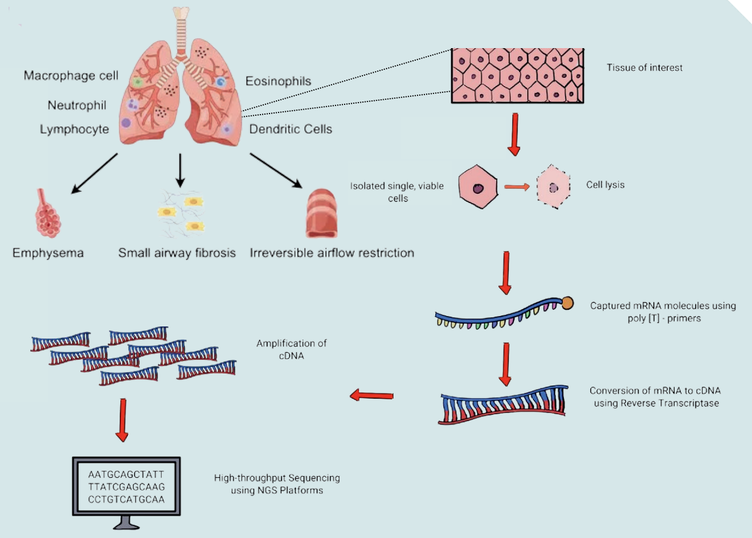


Figure 1: Experimental workflow for RNA-seq–based transcriptomic profiling of COPD and control lung tissues.

Methods

Bioinformatics Workflow

Data source
Public RNA-seq dataset (Kim et al., 2015, DOI: 10.1155/2015/20693

Differential Expression Analysis
DESeq2

Gene Annotation
BiomaRt

Visualization
Volcano plot, Heatmap, Box Plot

Figure 2: Workflow of RNA-seq data processing and analysis for differential gene expression in COPD.
Schematic overview of the analytical pipeline used to identify differentially expressed genes between COPD and control lung tissues. RNA-seq data were obtained from a public dataset (Kim et al., 2015; DOI: 10.1155/2015/20693). Differential expression analysis was performed on 16,676 genes using DESeq2 in R. A total of 2,312 genes were identified as significantly differentially expressed (FDR < 0.01). Data visualisation was carried out using the ggplot2, pheatmap, biomaRt, reshape2, and ggrepel packages.

Differential Gene Expression in Lung Tissues

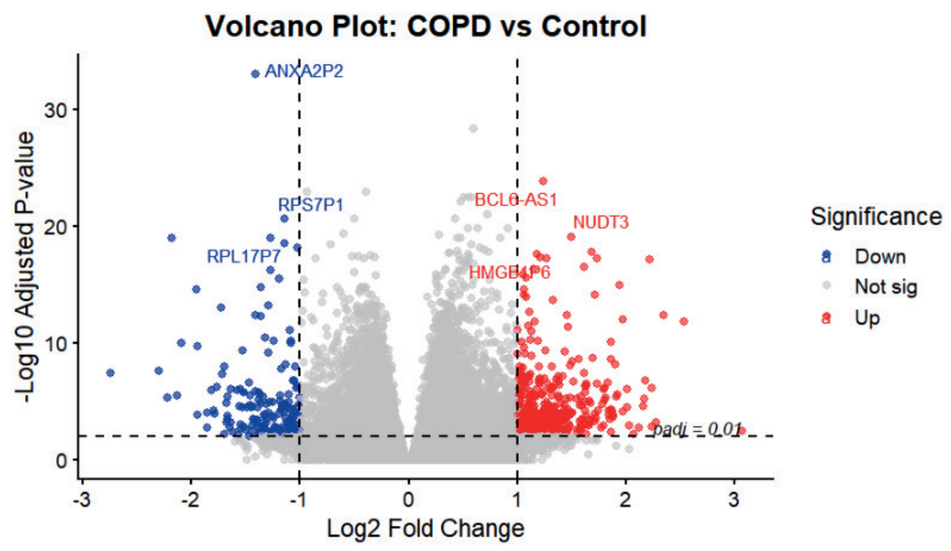


***Figure 3:** Volcano plot showing transcriptome-wide differential expression from RNA-seq analysis of lung tissues from subjects with COPD and matched healthy controls. Differential expression was assessed using the DESeq2 pipeline with the design formula ~ Disease after filtering for minimum read counts. The x-axis indicates log_2 fold change (COPD vs. control), and the y-axis shows $-log_{10}$ adjusted p-values (Benjamini–Hochberg correction). Genes with $|log_2FC| > 1$ and adjusted $p < 0.01$ are highlighted in red (upregulated in COPD) or blue (downregulated), while nonsignificant genes appear in gray. Dashed lines mark statistical thresholds. The results reveal significant upregulation of oxidative stress–related and chromatin-modifying genes and downregulation of metabolic and structural genes, reflecting key molecular alterations associated with COPD progression.*

Top 50 Differentially Expressed Genes



***Figure 4:** Heatmap showing relative expression patterns of the 50 most significantly differentially expressed genes identified by DESeq2 analysis of RNA-seq data from lung tissues of subjects with COPD and healthy controls. Genes were filtered for minimum expression and ranked by adjusted p-value. Variance-stabilizing transformation (VST) was applied to normalized counts, and expression values were mean-centered and scaled by row to emphasize relative differences. Columns represent individual samples (COPD or control), and rows correspond to genes ranked by significance. Hierarchical clustering using Euclidean distance and complete linkage revealed distinct sample groupings. Red indicates higher, and blue indicates lower relative expression. COPD samples clustered separately from controls, demonstrating robust transcriptional divergence. Upregulated genes (e.g., NUDT3, BCL6-AS1) were linked to oxidative stress and chromatin remodeling, while downregulated genes (ANXA2P2, RPS7P1) were associated with metabolic and structural pathways.*

Differential Expression of ANXA2P2 and BCL6-AS

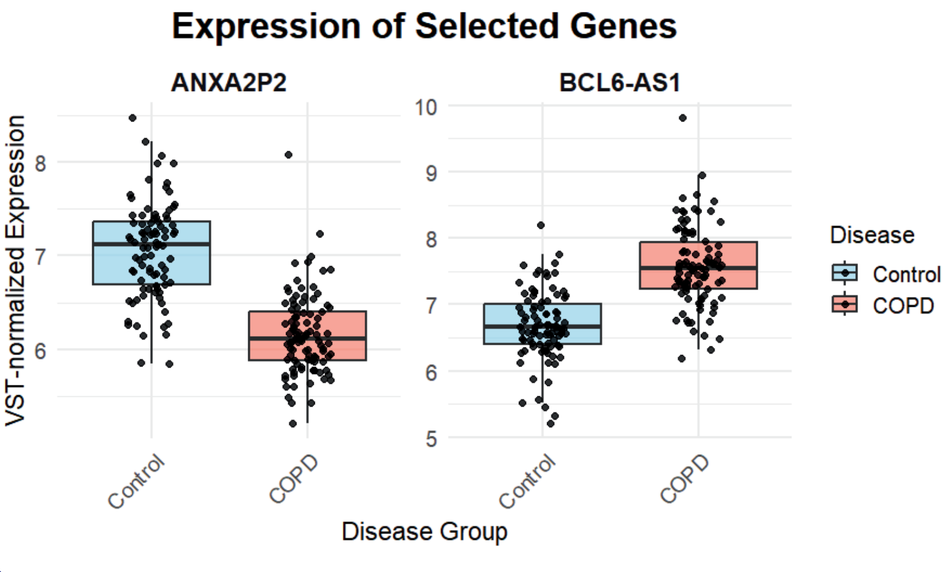


***Figure 5:** Boxplots show VST-normalized RNA-seq expression levels of ANXA2P2 and BCL6-AS1 in lung tissues from subjects with COPD (red) and healthy controls (blue). Expression values were obtained from DESeq2 analysis after variance-stabilizing transformation and normalization of raw counts. Each point represents an individual sample, and boxplots indicate the median and interquartile range. ANXA2P2 expression was significantly lower, whereas BCL6-AS1 expression was significantly higher in COPD compared with controls (adjusted $p < 0.05$, DESeq2 Wald test). These patterns highlight opposing regulation of genes linked to metabolic and chromatin remodeling pathways in COPD.*

Conclusion

Analyses reveal clear transcriptional differences between COPD and control lung tissues, reflecting distinct molecular mechanisms. ANXA2P2 is downregulated, while NUDT3 and BCL6-AS1 are upregulated in COPD, indicating disrupted metabolic, oxidative stress, and chromatin remodeling pathways. Heatmaps and boxplots confirm these inverse expression patterns, with COPD samples clustering separately from controls.

Functionally, BCL6 regulates inflammation and neutrophil survival, NUDT3 protects against oxidative stress and supports DNA repair, and ANXA2P2/AnxA1 modulates inflammation and fibrosis. Dysregulation of these genes contributes to chronic inflammation, tissue remodeling, and disease progression in COPD, and also links to lung cancer development. These findings highlight key molecular drivers of COPD and potential therapeutic targets.

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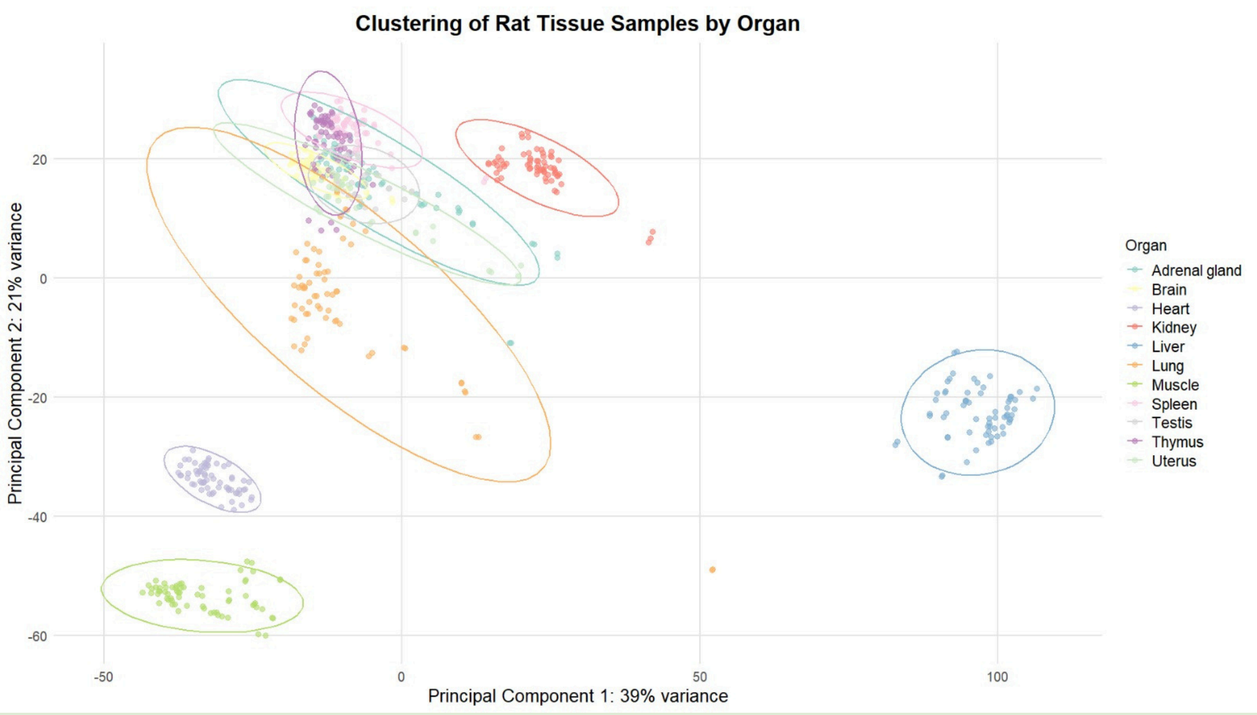
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SEX- AND AGE-DEPENDENT GENE EXPRESSION IN RAT HEART TISSUE

T. Broeren
H. Overkamp
A. Roncoli
C. Popa
L. Pranger
A. Rui

Introduction

Gene expression profiles change over time as organisms grow, develop, and age (Glass et al., 2013). Other sources of variation in gene expression are caused by sex differences and hormones (Oliva et al., 2020). By studying the most up- and down-regulated genes across age for each gender, we can investigate how these two biological factors interact and alter gene expression. Sex and age are two major risk factors in cardiovascular disease (Rodgers et al., 2019). Differences in heart disease onset patterns and response to treatment are observed between men and women. Identifying the most up- or down-regulated genes can show which pathways are activated or suppressed in cardiac diseases, and how these pathways differ between sex and developmental stage. Unravelling how sex and age influence gene expression can aid in understanding when certain therapies work best and in developing more targeted therapies.

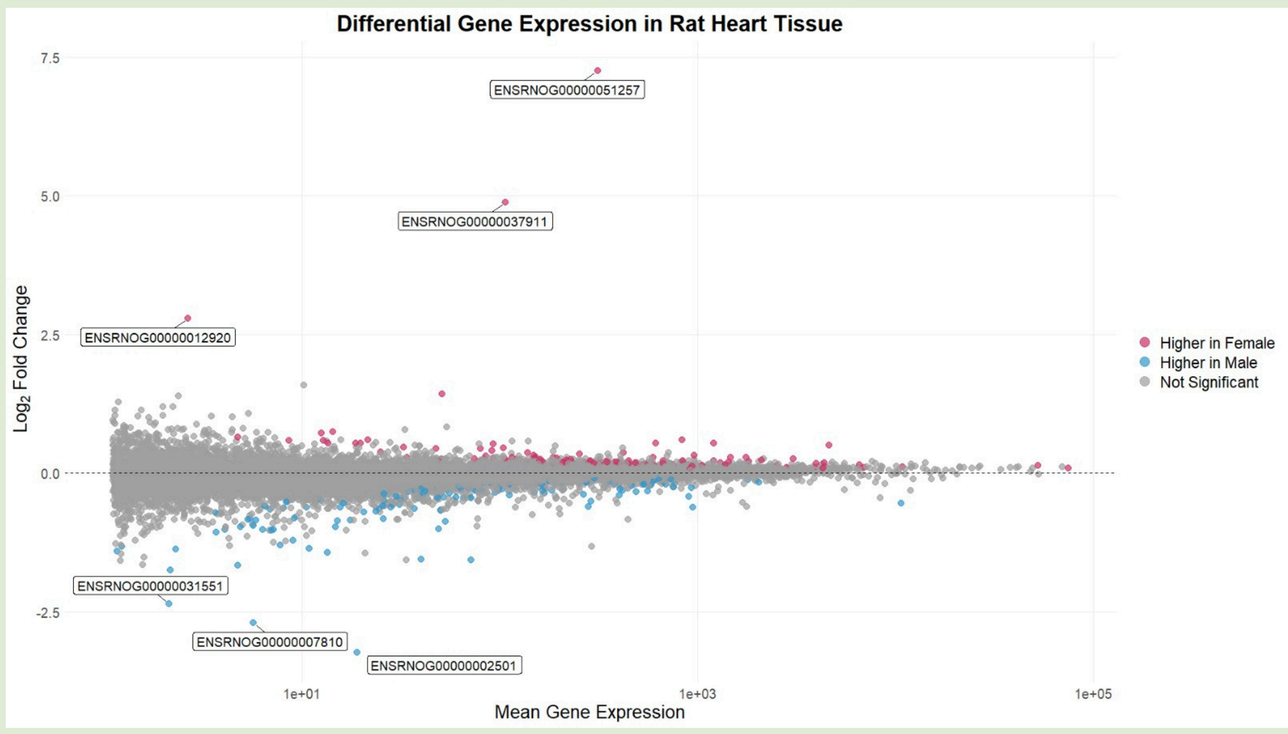


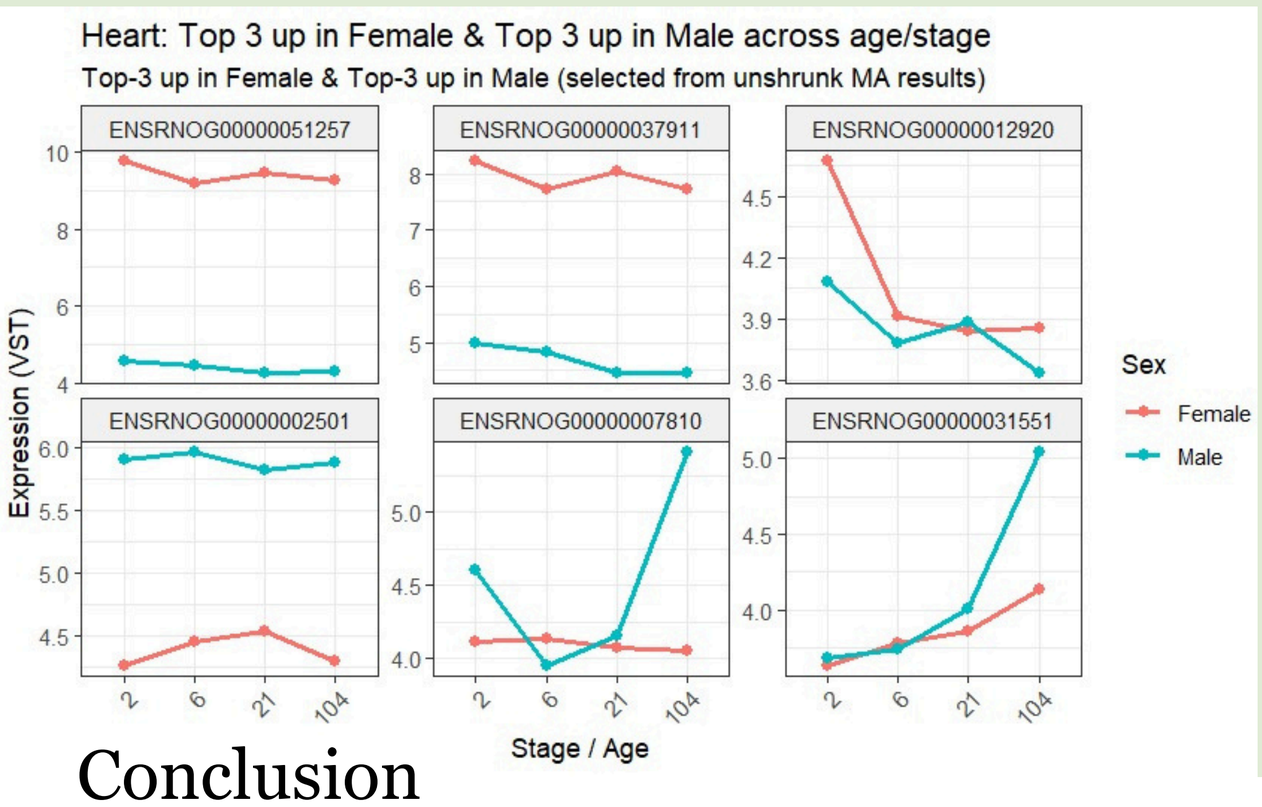
Which organ shows the most distinct and consistent gene expression pattern?

Figure 1. Principal component analysis of gene expression in different rat organ tissues. Data was normalised with variance stabilizing transformation (VST) method. A principal component analysis (PCA) plot was made to visualize the different tissue gene expression, with PC1 (39% variance) and PC2 (21% variance) explaining 60% of the variance. The plot shows close clustering of the data for the adrenal gland, brain, kidney, lung, spleen, testis, thymus and the uterus in the top left corner. The liver shows close clustering of data points, but shows more variation from the other organs. The muscle and the heart also show clustering further away from the other organs, with the heart samples showing the closest clustering of all organs.

Which genes are differentially expressed between male and female rat hearts?

Figure 2. Differential gene expression between male and female rats in heart tissue. Gene expression counts were normalized using the variance stabilizing transformation (VST). The log2 fold change of mean expression in females relative to males is plotted against the log10 of the average gene expression. The 143 genes expressed significantly higher in females (adjusted $p < 0.05$) are shown in red, and the 156 genes expressed significantly higher in males (adjusted $p < 0.05$) are shown in blue. P-values were adjusted for multiple testing using the Benjamini-Hochberg method. The three genes most highly expressed in females relative to males, and the three genes most highly expressed in males relative to females, are labeled.





How do sex-biased genes in the heart change across the lifespan?

Figure 3. Differential gene expression analysis in heart samples using DESeq2 (female vs. male). From the MA plot results, the three genes with the largest positive log2 fold change (higher in females) and the three with the most negative log2 fold change (higher in males) were selected. For each selected gene (one facet per gene), lines and points show the mean variance-stabilized expression (VST) per stage/age for each sex; y-axes are free per panel, and stages are ordered chronologically. Colors indicate sex: female = red and male = blue. Top row facets correspond to genes upregulated in females; bottom row facets correspond to genes upregulated in males.

Conclusion

-Gene expression in rat heart tissue differs between sexes, with 156 genes higher expressed in males and 143 in females

-Gene expression patterns differ between sexes and change with age: in females, some genes remain stable while others decrease with aging, reducing sex differences; in males, several genes vary over time, with some maintaining consistently higher expression or showing stronger age-related increases compared to females.

-The most sex-biased genes identified are not involved in heart disease, indicating that while sex influences gene expression, disease-related genes show no major sex differences under normal conditions.

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Investigating Core Senescence Genes in Irradiated Keratinocytes

university of groningen

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INTRODUCTION

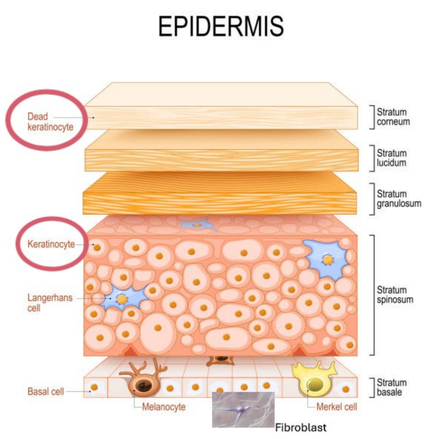


Figure 1. Structure of the human epidermis and localization of major skin cell types.

- Senescence is a stable growth arrest with heterogenous transcriptomes
- Dataset retrieved from Hernandez et al., 2017 where fibroblasts, keratinocytes and melanocytes were profiled at different timepoints post irradiation
- **Aim:** to identify potential senescence biomarkers in keratinocytes.

METHODS

- **Data & design:** RNA-seq raw counts from Hernandez et al., 2017, 6 reps per group, 78 in total
- **Pre-processing:**
  - removed lowly expressed genes (CPM ≥ 1 in ≥ 3 libraries)
  - normalisation (edgeR, TMM)
- **Model & differential expression:** GLM and QLF --> due to the negative binomial distribution of the dataset
- **Software**
  - **R** (v4.x), packages: edgeR, limma, pheatmap, ggplot2, dplyr, biomaRt, ggrepel

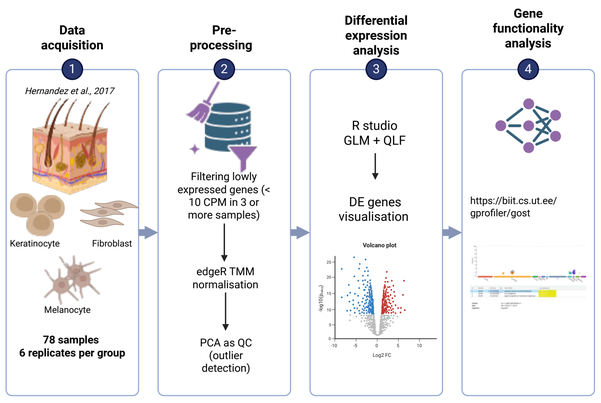


Figure 2. bioinformatics pipeline of our case study (created in biorender).

CONCLUSION

PTCHD4 can possibly be used as a biomarker for senescence in keratinocytes

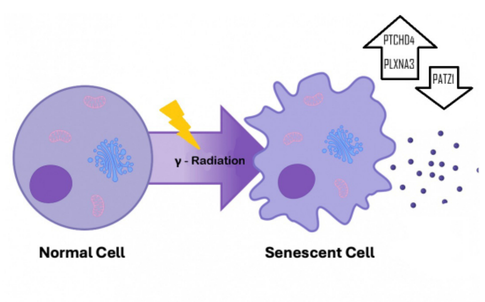


Figure 3. Induction of cellular senescence by γ-radiation and associated gene expression changes.

RESULTS

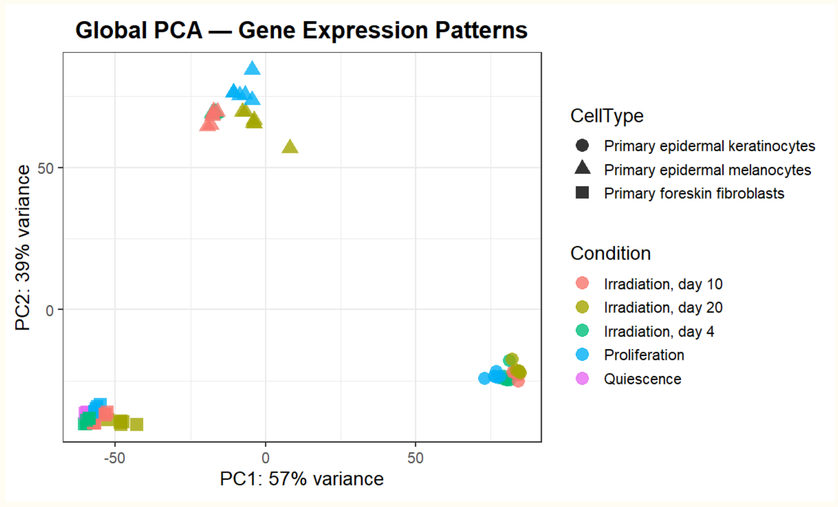


Figure 4. Principal Component Analysis (PCA) of global gene expression patterns across primary skin cell types and experimental conditions.
PCA was performed on normalized gene expression values to visualize overall transcriptional relationships between samples. Each point represents one biological sample, colored by experimental condition and shaped by cell type. The first two principal components (PC1 and PC2) explain 57% and 39% of the total variance, respectively. Distinct clustering indicates that both cell type and irradiation time contribute strongly to transcriptional variation.

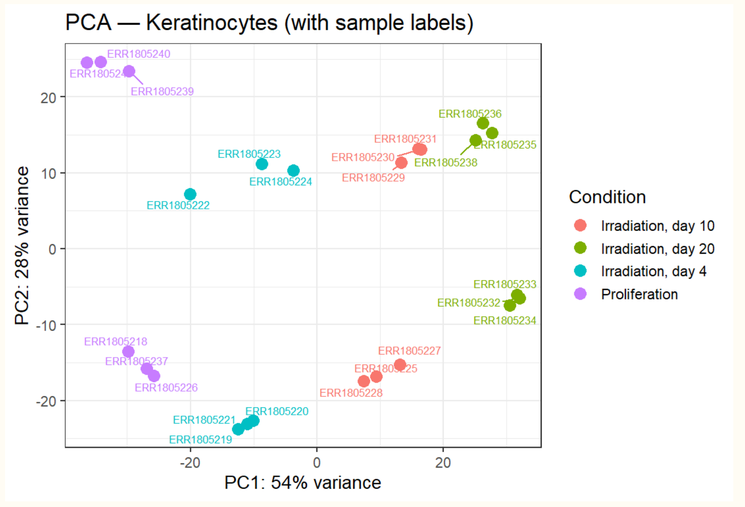


Figure 5.Temporal changes in keratinocyte transcription after irradiation.
PCA shows a temporal trajectory of keratinocyte transcription. Proliferating cells cluster at one extreme, Day 4–10 samples occupy intermediate positions with mixed proliferative and stress-response genes, and Day 20 samples form a distinct cluster, reflecting stable senescence. Clusters are divided into two groups, likely due to batch effects arising from technical variation.

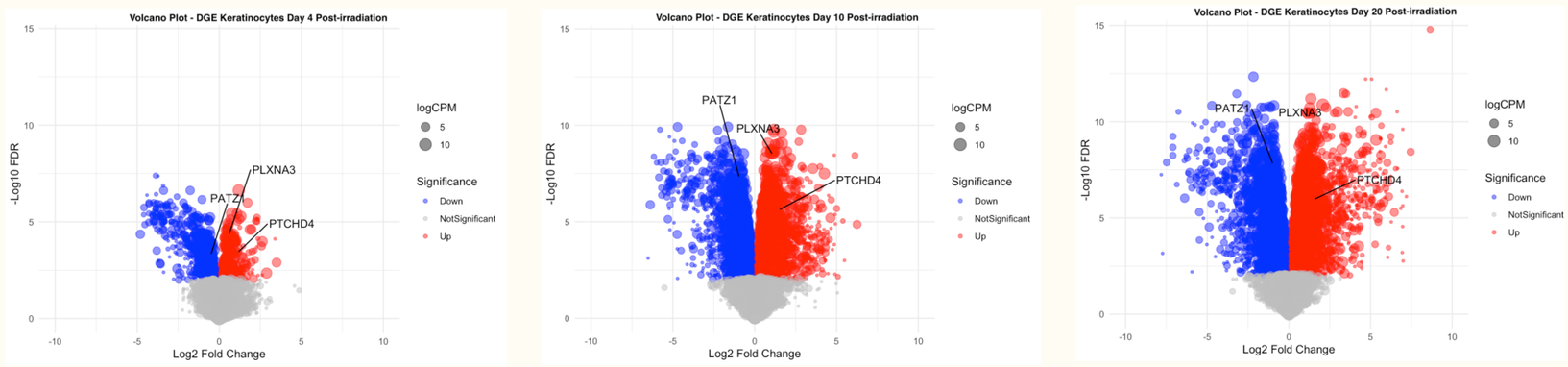


Figure 6. Volcano Plot of differential gene expression in keratinocytes at Day 4, 10 and 20 post-irradiation. The plot shows Log_2 Fold Change (x-axis) versus $-Log_{10}$ FDR (y-axis), representing the magnitude and significance of expression changes relative to Day 1 (proliferation). Red and blue points indicate significantly upregulated and downregulated genes, respectively, while grey points represent non-significant changes. Circle size represents gene expression level shown as logCPM.

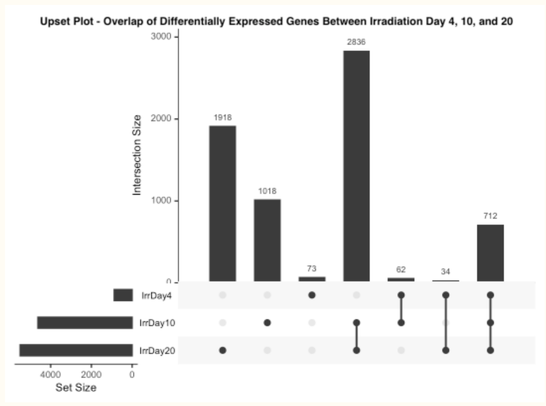


Figure 7. Upset Plot depicting the number of overlapping significantly differentially expressed genes across irradiation timepoints in keratinocytes.
For selecting significantly expressed genes the FDR cut-off is 0.01.

- Differential gene expression increases with time post-irradiation
- PATZ1, PLXNA3, PTCHD4, are significantly differentially expressed, increasing in significance while maintaining similar expression levels
- These genes have been shown to be involved in senescence-linked pathways, supporting their role in inducing a senescence state in keratinocytes in response to radiation
- Days 10 and 20 post-irradiation show the most shared significantly differentially expressed genes
- Day 4 is the closest to proliferation state, shown by the low number of differentially expressed genes compared to the reference point

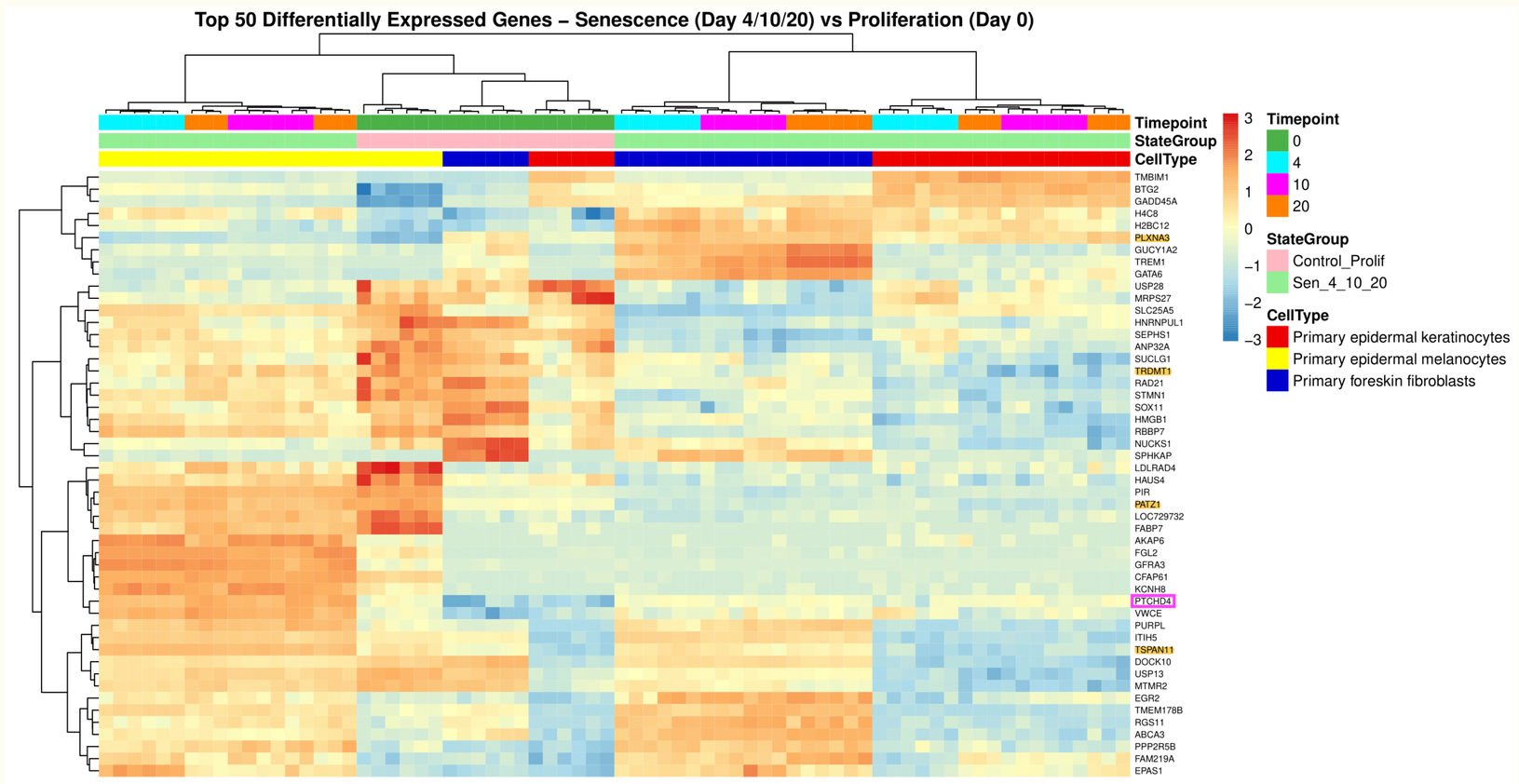


Figure 8. Heatmap of the top 50 significantly DE genes across the 3 different cell types (Melanocytes, Fibroblasts, Keratinocytes) in irradiated against proliferation state. Columns are clustered and annotated. Genes are shown in the rows, and columns are samples. Few notable senescence core genes are PATZ1, PLXNA3, PTCHD4, TRDMT1, TSPAN11. Z-score scaling: comparing the differences of each gene expression from its mean across all the samples.

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THE EFFECT OF COPD ON GENE TRANSCRIPTION

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	COPD subjects	Control subjects	*P* value
Male, *n* (%)	98 100.0	91 100.0	
Age, years	67.5 ± 6.4	60.9 ± 9.5	<0.0001
Smoking (py)	48.0 ± 22.0	35.2 ± 17.2	<0.0001
FEV1, %	71.9 ± 13.4	91.0 ± 12.4	<0.0001
FEV1/FVC	57.1 ± 7.8	74.8 ± 4.3	<0.0001
DLCO, %	77.4 ± 13.8	92.8 ± 13.2	<0.0001

COPD: chronic obstructive pulmonary disease; DLCO: diffusing capacity of the lung for CO_2; pack-years; FEV1: forced expiratory volume in 1 second. Unless otherwise stated, the mean ± standard deviation is shown.

INTRODUCTION

- CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IS A GROUP OF DISORDERS THAT IMPAIR LUNG FUNCTION (ALFAHAD ET AL., 2021).
- ASSOCIATED CONDITIONS INCLUDE EMPHYSEMA, DAMAGE TO ALVEOLAR WALLS, AND CHRONIC BRONCHITIS (ZHANG ET AL., 2021).
- IT AFFECTS AN ESTIMATED 65 MILLION PEOPLE WORLDWIDE, CAUSING ABOUT 3 MILLION DEATHS ANNUALLY (WHO., 2024).
- COMMON SYMPTOMS INCLUDE SHORTNESS OF BREATH, CHRONIC COUGH, AND PROGRESSIVE LOSS OF LUNG FUNCTION.
- MAJOR RISK FACTORS INCLUDE CIGARETTE SMOKING, OCCUPATIONAL EXPOSURE, BIOMASS SMOKE, AND, MORE RECENTLY, NORMAL AGEING (LANGE ET AL., 2015).

PCA Plot Control vs COPD

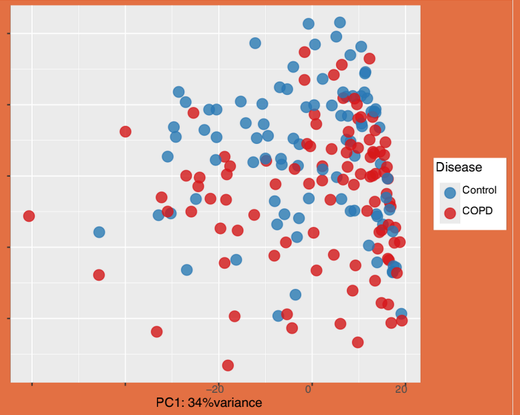


Figure: Principal component analysis of RNA sequencing data. PC1 is on the x-axis (34% variance) and PC2 is on the y-axis (14% variance). Each point represents a sample, colored by COPD (Red) vs control (Blue).

Interesting genes:

ANXA2P2
FTH1
GALNT4
FGG
Genes involved in aerobic electron transport chain

Vulcano plot of Top 10 Up & Down Regulated Gene Expression in Control vs COPD

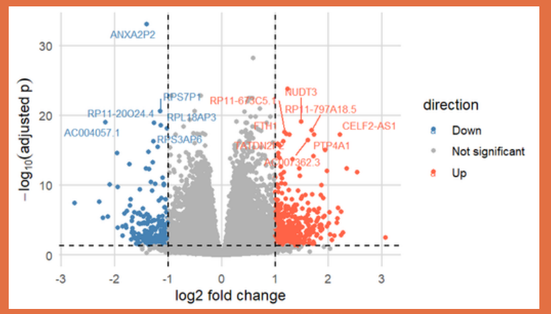


Figure Volcanoplot: X-axis portrays the change in expression between COPD and Controls. Y-axis shows significance of difference as log-10(adjusted p-value)(adjusted for mulitple testing error). Top 10 most significant upregulated and downregulated genes are anotated on either side.

Heatmap of Top 10 Up & Down Regulated Genes in Control vs COPD

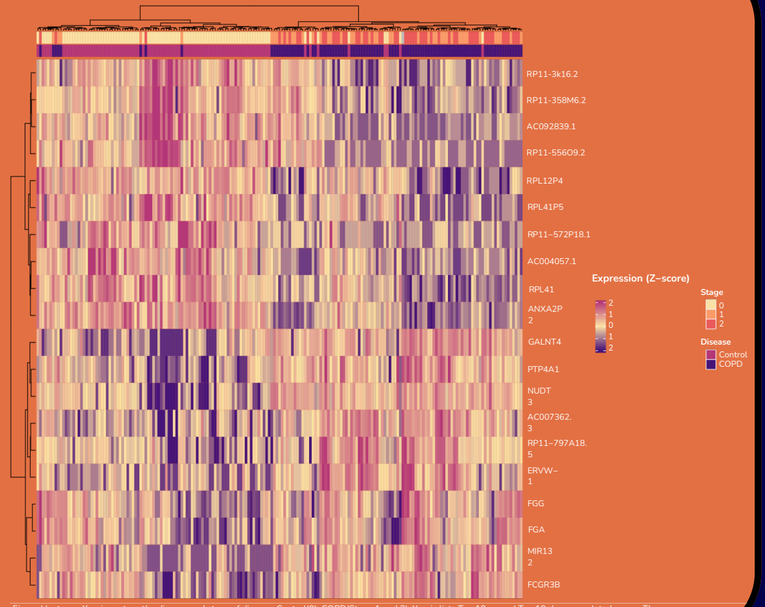
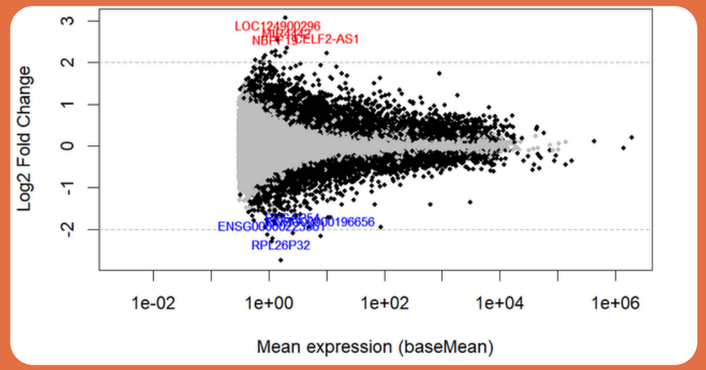


Figure Heatmap: X-axis portays the disease and stage of disease: Control(0), COPD(Stage 1 and 2). Y-axis lists Top 10 up and Top 10 down regulated genes. These genes are significantly changed in regulation. Top 10 Up and Top 10 Down regulated genes are selected based on their log expression values.

MA plot of Control VS COPD



Most relevant genes

Gene code	Fold change	Regulation	Full gene name
RPL26P32	-2.744448	downregulated	Ribosomal Protein L26 (RPL26) Pseudogene
NA	-2.294202	downregulated	NA
NA	-2.175427	downregulated	NA
RPSAP54	-2.091723	downregulated	Ribosomal Protein SA Pseudogene 54
NBPF19	2.178271	upregulated	Neuroblastoma Breakpoint Family Member 19
CELF2-AS1	2.218741	upregulated	CELF2 Antisense RNA 1 (Non-Protein Coding)
MIR4442	2.343535	upregulated	MicroRNA 4442
LOC124900296	2.532783	upregulated	Small Nucleolar RNA SNORA19

Figure: The MA plot shows the difference between the two groups on the Y-axis, and the average of expression in the X-axis

CONCLUSION

- FGG, FGA, AND PTP4A1 FORM A STRONGLY CONNECTED CLUSTER, SUGGESTING A MECHANISTIC SHIFT IN CELLULAR DIFFUSION AND RESULTING IN FIBRIN DEPOSITION.
- FTH1 MAY INDICATE MITOCHONDRIAL DYSREGULATION, AS SEVERAL DOWNREGULATED GENES ARE LINKED TO THESE PROCESSES.
- GALNT4 PROMOTES MUCIN HYPERSECRETION, INFLUENCING CELL PROLIFERATION AND INVASION (GUO ET AL., 2025).
- FGG HAS BEEN REPEATEDLY IDENTIFIED AS A POTENTIAL COPD BIOMARKER (ZHANG ET AL., 2021; KIM ET AL., 2015).
- COLLECTIVELY, THESE GENES ARE ASSOCIATED WITH INFLAMMATORY RESPONSES SIMILAR TO CHRONIC BRONCHITIS (YU ET AL., 2021), APPEAR TO DRIVE DISEASE PROGRESSION, AND INDICATE ALVEOLAR CELLULAR DYSFUNCTION, THOUGH THEIR SPECIFIC ROLES REQUIRE FURTHER INVESTIGATION.

REFERENCES

Team 10

Amygdala Gene Expression Under Death Circumstances

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Introduction

The amygdala is responsible for processing external stimuli and generating emotional responses. Particularly in response to fear, it is also capable of storing fear memories (1,2). Consequently, fear can also lead to physiological changes in the amygdala, such as gene expression (3). Therefore, we aim to investigate how a prolonged period of dying can impact gene expression in this brain region and identify common pathways affected by this process. To achieve this, data from the GTEx portal were retrieved, and the gene expression in the amygdala of patients who experienced a sudden death (group 1) was compared to those who had suffered a prolonged death (group 4). This research revealed that certain genes were upregulated in longer cases of death with variance in the affected transcription patterns based on age.

Material & Methods

Data from the GTEx Portal were used, including amygdala gene read counts and brain sample metadata (gender, age, cause of death, and sampled organs). The dataset was filtered to include only amygdala samples from individuals who experienced violent fast or slow deaths, and files were merged using donorID. Analyses were conducted in RStudio, generating a volcano plot, heatmap, and boxplots (see QR code for script).

Results & Discussion

Differential gene expression in the amygdala comparing violent, fast death to slow death.

The volcano plot for the differential gene expression showed us several up- and down-regulated genes. A literature review was conducted to gain a deeper understanding of the function of the most differentially expressed genes with the highest P-value. **IL1RL1** is a receptor activated by the cytokine IL-33, which is released from damaged cells, thereby initiating an early inflammatory response (4). During inflammation, **SERPINA3** is upregulated to counteract proteolytic activity and prevent tissue destruction (5). **KIF19** expression increases during prolonged cellular stress, as there is cytoskeletal remodeling and alteration of the cilia-based signaling to maintain structural integrity (6). Meanwhile, **ENGS00000281383**, a gene whose function is mostly unknown, is similar to YY1, suggesting involvement in histone deacetylation and acetylation (7,8).

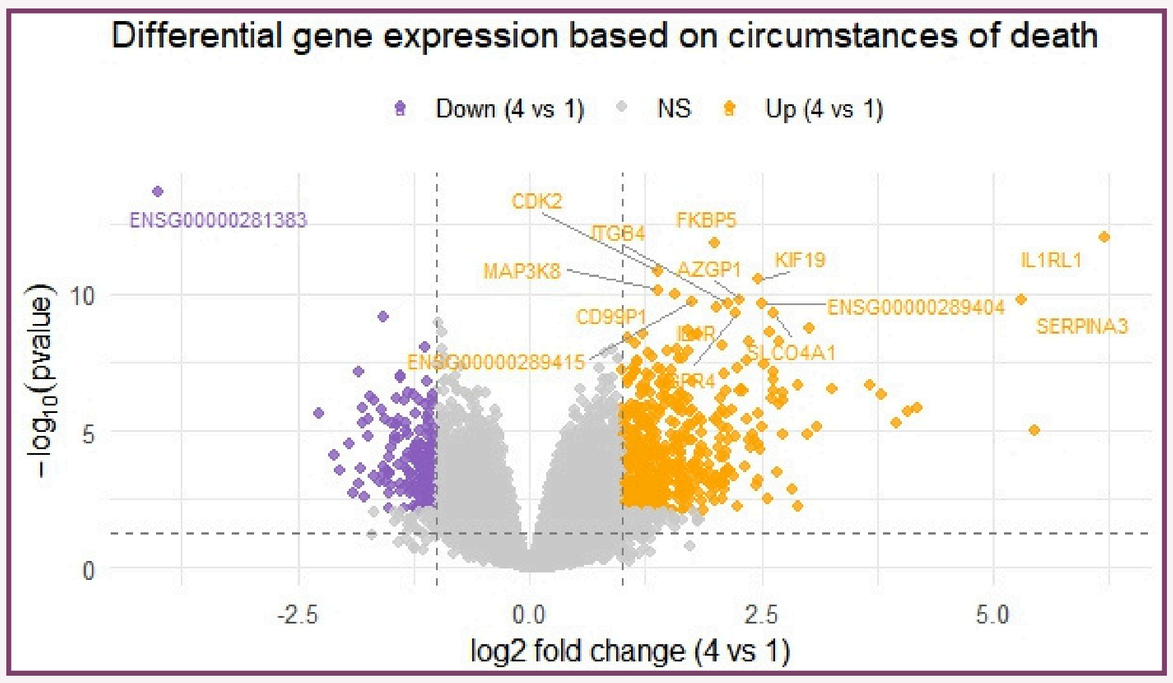


Figure 1: Volcano plot of differential gene expression in the amygdala when comparing violent and fast death to slow death. Colors indicate differential expression (fold change): purple = downregulation, yellow = upregulation. The threshold for log2fold change was set at -1 for downregulation and at 1 for upregulation. For the -log10(P-value), the threshold was set at 1. The most upregulated and significant genes are IL1RL1, SERPINA3, and KIF19, which are primarily involved in stress response and damage repair. The most downregulated gene is ENSG00000281383, for which the function is largely unknown; however, it is similar to YY1, suggesting involvement in histone acetylation.

Differential gene expression in the amygdala, comparing the z-score between different death circumstances.

Comparing the z-scores between violent and fast death versus slow death, several genes exhibit upregulation in violent and fast deaths. **ICRH** is a precursor to a neuropeptide hormone that is secreted to modulate homeostasis during stress (9). **HPCA** encodes a protein involved in phytosignal transduction and may reflect sensory/signal adaptation under stress (10). The function of **ENSG00000253553**, located on chromosome 8, is unknown. Meanwhile, genes such as MVP and TNFRSF6B are downregulated. These genes encode proteins that are involved in stress stabilization and cell survival (11,12).

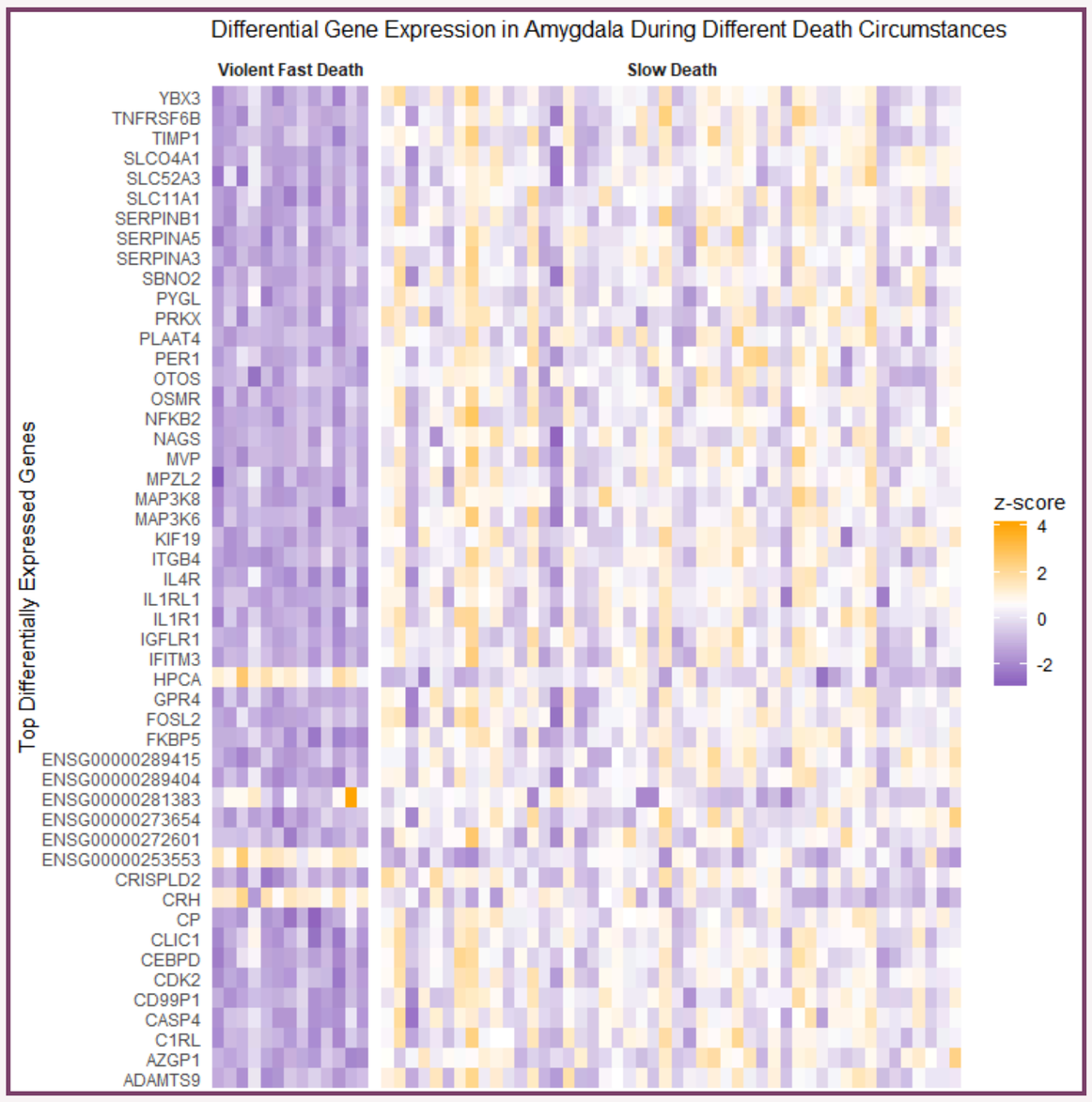


Figure 2 : Heatmap of differential gene expression in the amygdala from individuals experiencing violent fast death (left) versus slow death (right). Colors indicate relative expression (Z-scores): purple = downregulation, yellow = upregulation. TNFRSF6B and MVP are upregulated in slow deaths, reflecting prolonged stress and survival signaling, while their downregulation in fast deaths suggests acute injury or cell loss. Neuronal genes such as HPCA and CRH show distinct patterns, highlighting altered neuroendocrine and stress-response activity between conditions.

Differential gene expression in sex and age

Other than speed of death, donors also differed in two other categories within the dataset, these being sex and age. To examine whether these other variables impact the differential gene expression between quick and long death conditions, a DGE analysis was performed on the groups individually. Genes with high differential expression and significance were then plotted to examine possible differences. Results showed that sex does not significantly impact DGE in both downregulated and unregulated genes. Age however did seem to have an impact, specifically, in the age range 70-79, far more genes were differentially expressed than in other age groups.

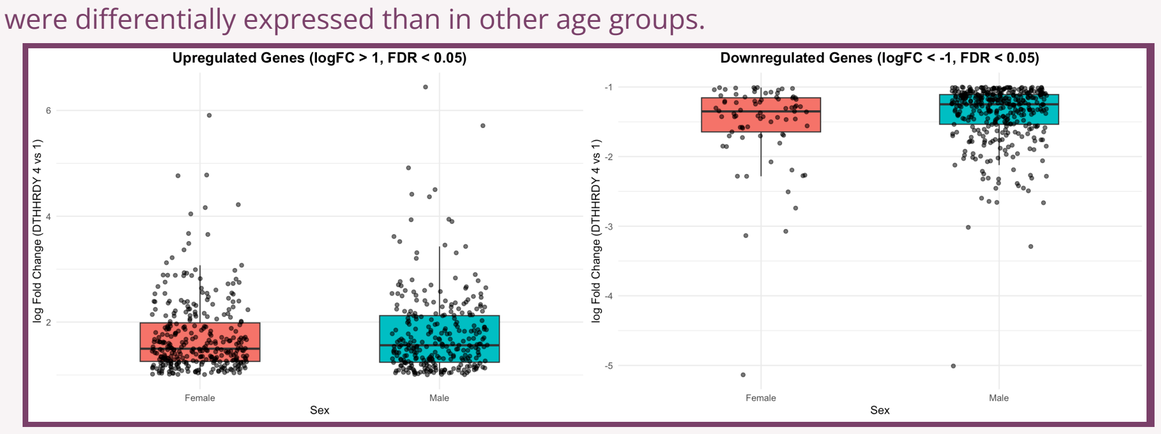


Figure 3A: Boxplots showing significantly differentially expressed genes (|logFC| > 1, FDR < 0.05) between DTHHRDY 1 and 4 in males and females. Left plot shows upregulated genes, right plot shows downregulated genes.

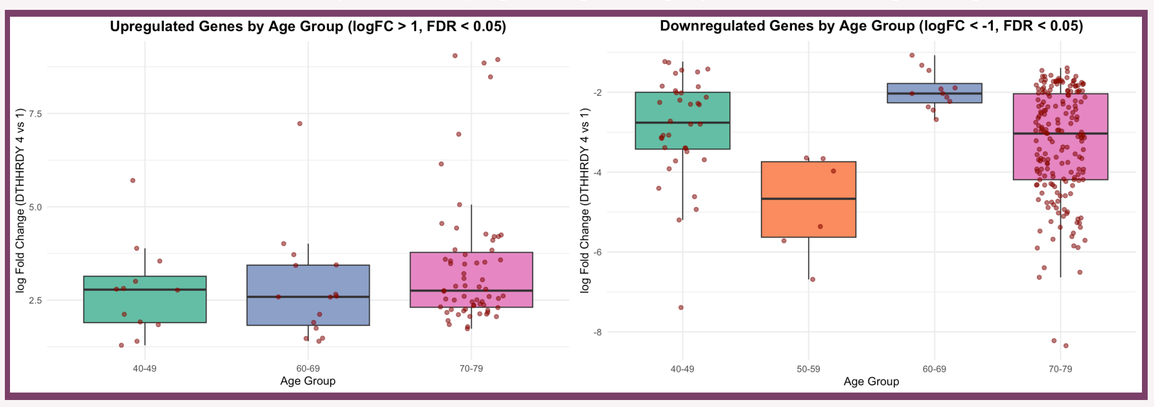


Figure 3B: Boxplots showing significantly differentially expressed genes (|logFC| > 1, FDR < 0.05) between DTHHRDY 1 and 4 in varying age groups. Left plot shows upregulated genes, right plot shows downregulated genes. Age groups not represented on graph had no genes that passed the set thresholds.

Conclusion

Prolonged death appears to significantly alter gene expression in the amygdala, specifically in pathways related to stress, inflammation and cellular adaptation. The results of this poster show increased activity in genes involved in inflammatory signaling and cytoskeletal remodeling, alongside reduced expression of genes linked to cellular stability and survival. Age, but not sex, influenced these transcriptional patterns, with older individuals showing greater variability. These findings suggest that extended physiological distress causes characteristic molecular changes in the amygdala, highlighting the way prolonged dying impacts brain function at the end of life.

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RStudio code | References | Contact Info

Transcriptomic Profiling of COPD Lung Tissue Reveals Dysregulation in Proteasome and Oxidative Phosphorylation Pathways

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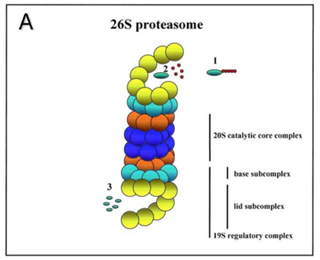
INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung disorder characterized by airflow limitation, inflammation, and tissue remodeling. At the molecular level, COPD is associated with **cellular stress, mitochondrial dysfunction, and impaired protein turnover**.

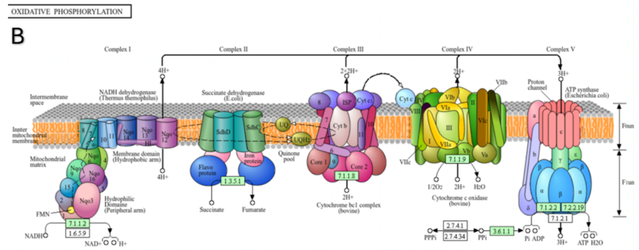
We aim to identify **key genes and pathways dysregulated in COPD lung tissue compared to control non-COPD lung tissue**, with a focus on two functional categories:

1. **Proteasome-related genes:** mediators of protein degradation, whose dysfunction can lead to accumulation of damaged proteins and increased cellular stress.
2. **Oxidative phosphorylation (OXPHOS) genes:** critical components of mitochondrial energy metabolism, often downregulated under oxidative stress conditions.

Proteasome and Oxidative phosphorylation

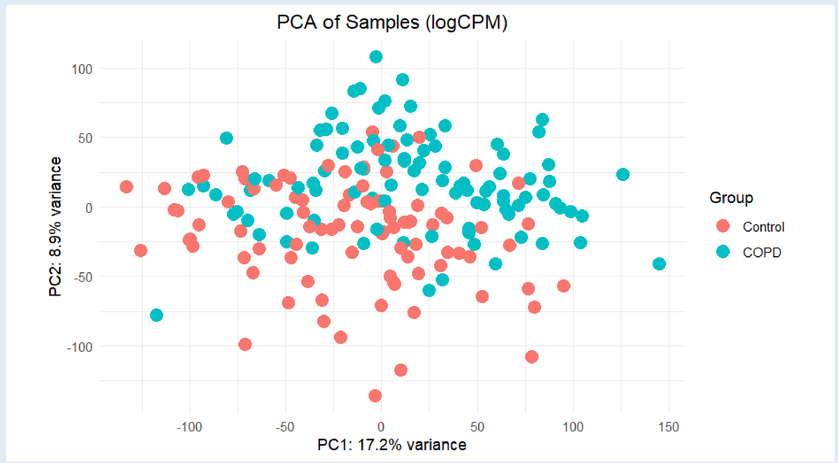


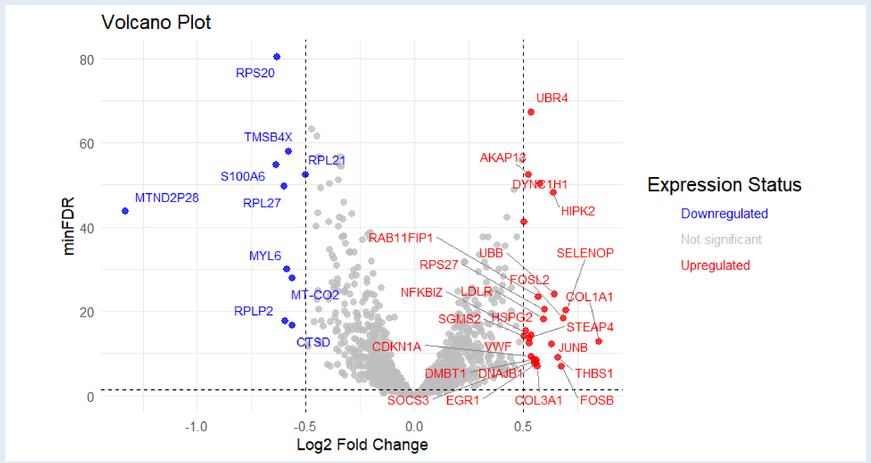
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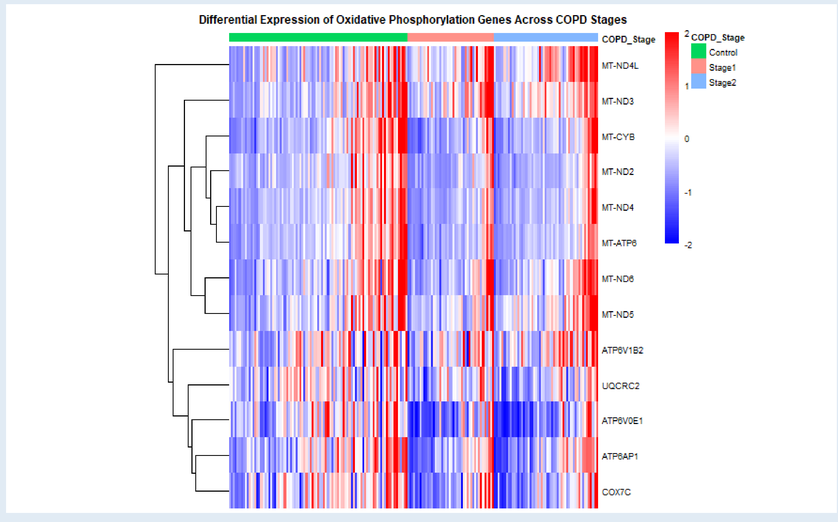


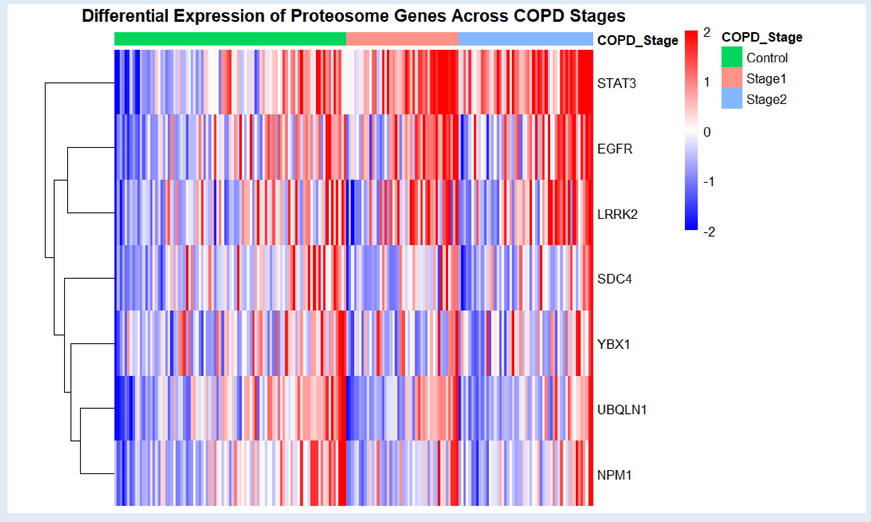
(KEGG PATHWAY: Oxidative Phosphorylation - Homo Sapiens (Human), n.d.)

RESULTS









Discussion

- Oxidative phosphorylation genes differentially regulated in COPD
  - **ATPV0E1** couples proton translocation to ATP synthesis in the mitochondrial membrane, enabling efficient energy production. Its downregulation in COPD likely causes a reduction in ATP production and disrupts pH regulation, impairing lung cell repair and accelerating disease progression.
  - **MT-ATP6** forms a proton channel in the mitochondrial inner membrane, driving ATP synthase rotation and enabling ATP production. Its downregulation in COPD could impair oxidative phosphorylation, by reducing ATP synthesis, and increasing ROS, potentially worsening lung cell damage and disease progression.
  - **MT-ND4L** is a transmembrane subunit of complex I (NADH dehydrogenase). Transfers electrons from NADH to ubiquinone. Upregulation could be a possible compensatory response to impaired electron transport chain function.
    COX7C is part of the mitochondrial respiratory chain complexes. It catalyzes electron transfer from cytochrome c to oxygen. Downregulation may indicate mitochondrial dysfunction, reduced ATP, and increased ROS.
- Proteasome genes upragulated in COPD lung tissue compared to the control
  - **STAT3** is a transcription factor that activates cytokines and growth factors. It is involved in cell survival, proliferation, inflammation and immune response.
  - **EGFR** is a receptor tyrosine kinase, activated by growth factos. It controls cell proliferation, differentiation, survival and tissue repair.
  - **LRRK2** is a serine/threonine kinase that functions in vesicle trafficking, autophagy and immune responses, and cytoskeleton dynamics

Conclusion

There are several significant changes in the proteasome pathway show an upregulated gene expression. This is a possible contribution to the progression of COPD. COPD may also be associated with broad mitochondrial dysfunction in several components of the electron transport chain, leading to energy deficits, oxidative stress, and eventual apoptosis.

ACKNOWLEDGEMENTS

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Our code:
https://docs.google.com/document/d/19XzREp-WF7chzI4YwTThQnKzoRTAemhNXs3wcFFkgBY/edit?usp=sharing

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From emotions to thoughts: how the humain Brain is wired differently according to sex

Camilla Nedjari (S6459196), Roshni Esther Dutta (S4701712), Lotte Mulder (S4888626) ,
Berber Ziengs(S2957086), Emel Hyusein (S3820483), Derk Wiersma (S4897323)

TEAM 13

AIM

Investigate sex specific differences in gene expression across three brain regions, focusing on upregulated genes in females compared to males. This analysis provides insights into molecular mechanisms that may contribute to sex-based variability in brain function.

INTRODUCTION

The brain is a complex network of connected specialised regions.

- The amygdala, which plays a role in emotion processing, stress response, fear, and threat detection, shows distinct patterns of activation between males and females, often linked to sex-specific stress responses (1).
- The hippocampus, which is essential for memory formation, also exhibits structural and functional differences between sexes (4).
- Similarly, sex differences in the prefrontal cortex, which is responsible for cognition, decision making, social behavior, and motor control has been associated with estrogen signaling and its interaction with the amygdala (5).



Figure 1. Illustrative image of the brain and the regions studied (Amygdala, Frontal Cortex, Hippocampus).

GENE EXPRESSION

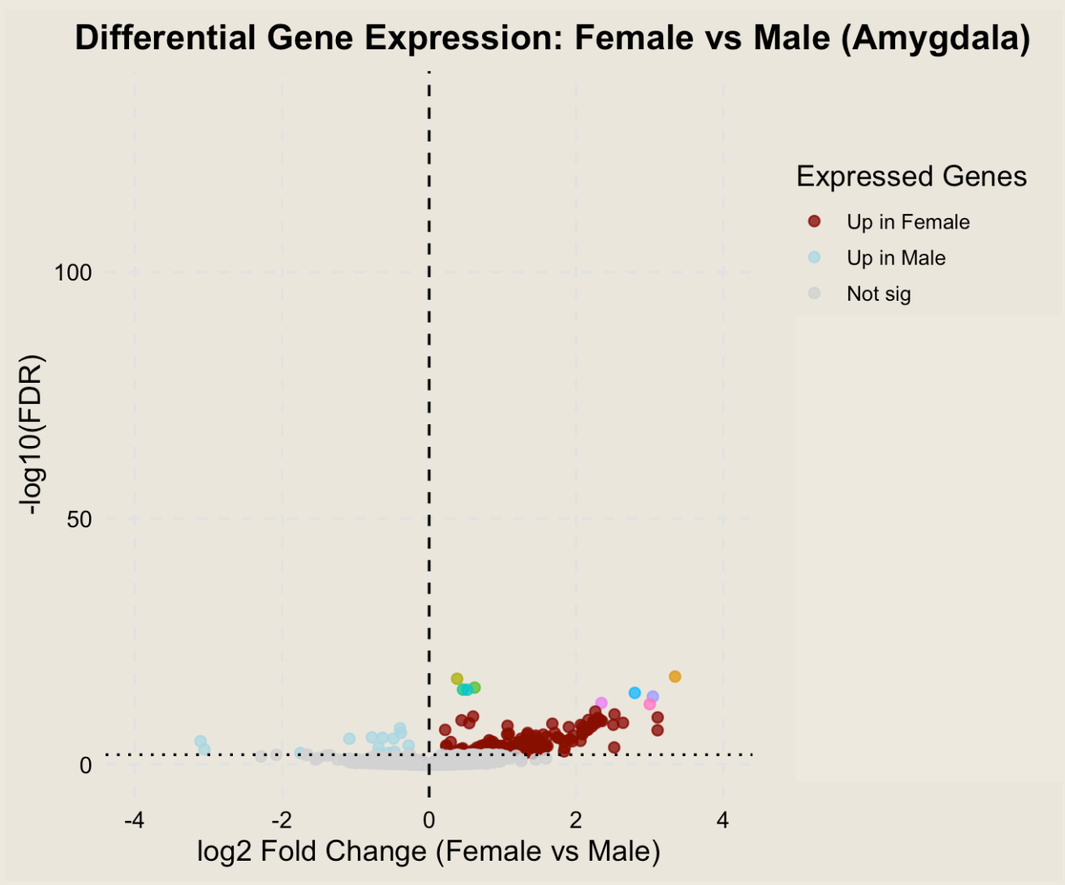


Figure 2: Volcano plot of the Differential Gene Expression in the Amygdala compared in males and females.
This volcano plot shows the differential gene expression in the amygdala between males and females. Each point represents a single gene, with females' genes marked in dark red and the males' genes marked in light blue. The highest genes on the plot have greater significance. This volcano plot allows us to identify the genes with statistically significant gender differences in amygdala expression.

CONCLUSION

- We identified several significantly differentially expressed genes between males and females in the brain.
- Male upregulated genes were mainly located on the Y chromosome, as expected since females lack this chromosome.
- The dataset included approximately three times more male than female samples; however, our statistical methods were robust enough to account for this imbalance.
- False Discovery Rate (FDR) correction was applied to minimize false positives and ensure reliability.
- Later in the analysis, comparisons across brain tissues revealed a substantial overlap in differentially expressed genes, indicating consistent sex-linked expression patterns.
- A few non–sex-linked genes also appeared significant, possibly due to donor-related factors such as disease history or cause of death.
- The cohort ranged from 21–79 years, so age-related gene dysregulation may have influenced expression profiles.
- Some upregulated genes may play important biological roles, warranting further investigation into their effects on brain function and sex-based differences in health.

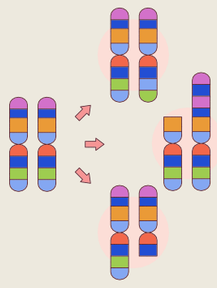
METHODS

- RNA-seq read count data and sample annotations for the amygdala, hippocampus, and frontal cortex were obtained from the GTEx database. The samples were grouped by sex (male and female).
- Genes with low expression (CPM < 1 in fewer than 3 samples) were removed. Normalisation and differential expression analysis were performed using the edgeR package, fitting a negative binomial model with sex as the main variable.
- Genes with a false discovery rate (FDR) below 0.01 were considered significantly differentially expressed. After which Ensembl gene IDs were mapped to gene symbols using biomaRt.
- Results were visualised using volcano plots, MA plots, PCA, and heat maps to explore overall expression patterns and sex-biased gene activity across the three brain regions.

HIGHLIGHTS



TPO & IYD are related to Thyroid activity in females



ZFX affects neuronal development and gene regulation in females

IGKV4-1 related to Immunoglobulin variable region; antibody diversity in females



NLGN4Y nervous system development linked to ASD in males



RESULTS

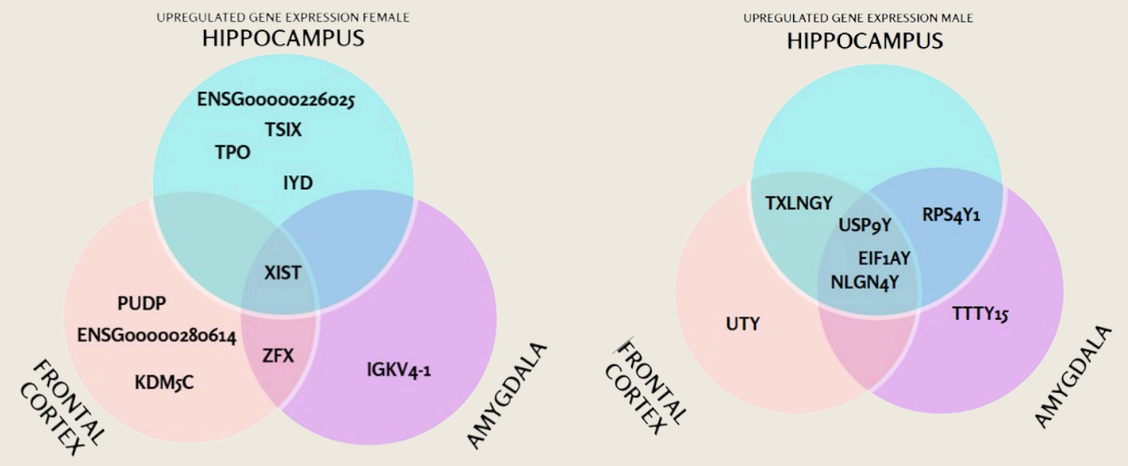


Figure 3. Sex-biased gene expression across hippocampus, amygdala, and frontal cortex.
RNA-seq data from the GTEx database were analyzed to identify genes upregulated in males and females across three brain regions. Venn diagrams show the distribution of significantly differentially expressed genes (FDR < 0.01) in each region. Circles represent the hippocampus, amygdala, and frontal cortex, with genes in intersections upregulated in multiple regions and genes in single circles upregulated in only one region. (A) Female-biased genes (B) Male-biased genes

AGING THROUGH ORGANS: *How Gene Expression Changes with Time*

Group 14: Anca Gorunescu, Bokke Bronswijk, Hielko Kasma, Esmée van Peer, Esmee Werkman, Kaj Mulder

To what extent does **gene expression** differ in certain organs depending on the **age of death**?

1. Data Grouping

- GTEx data for aorta, hippocampus and lung



2. Analysis

- Differential expression analysis with **DESeq2** (R library), **FDR-adjusted**.
- Functional enrichment of significant genes via **G:Profiler**.
- **PERMANOVA** on PCA distances to assess transcriptomic differences by age.

3. Visualization

- **Variance-stabilizing transformation**
- **PCA** to show age-dependent clustering
- Visualized with **volcano plots** highlighting significant genes.

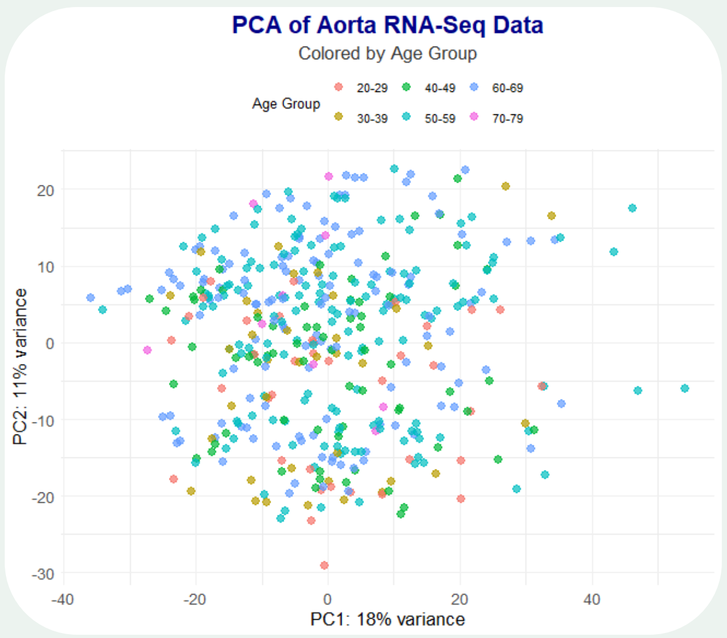
AORTA

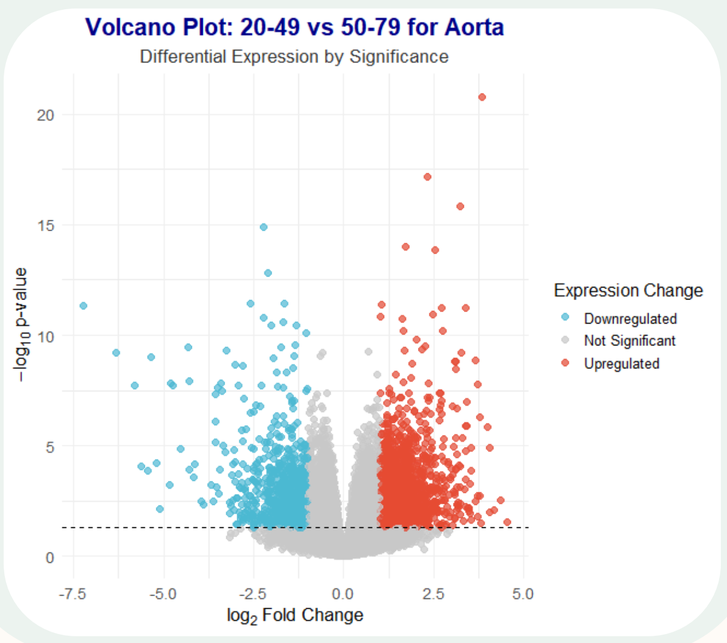
- **Vascular aging** contributes to **age-related CVD**s (Gao et al., 2020).
- In mice, **aging** increases **immune/inflammatory activity** and reduces **ECM integrity** and **stress response** (Gao et al., 2020).
- In primates, **longevity-related genes** are **downregulated with age** (Zhang et al., 2020).

Are the same differences present in humans?

PCA: No clear age-group clustering → major variance not age-driven (3.7%, p=0.001).

Volcano plot: Comparing Young (20–49) vs Old (50–79) shows significant up- (2049) and downregulated (889) genes.





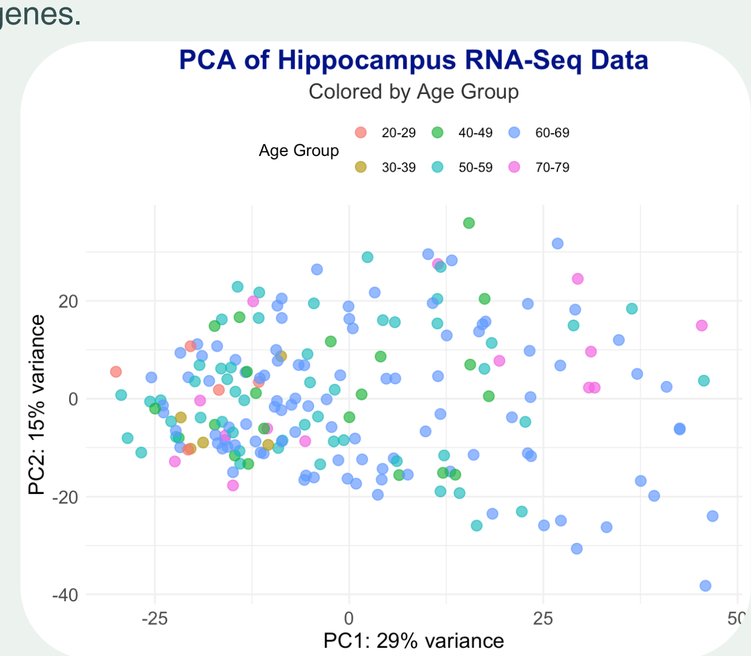
HIPPOCAMPUS

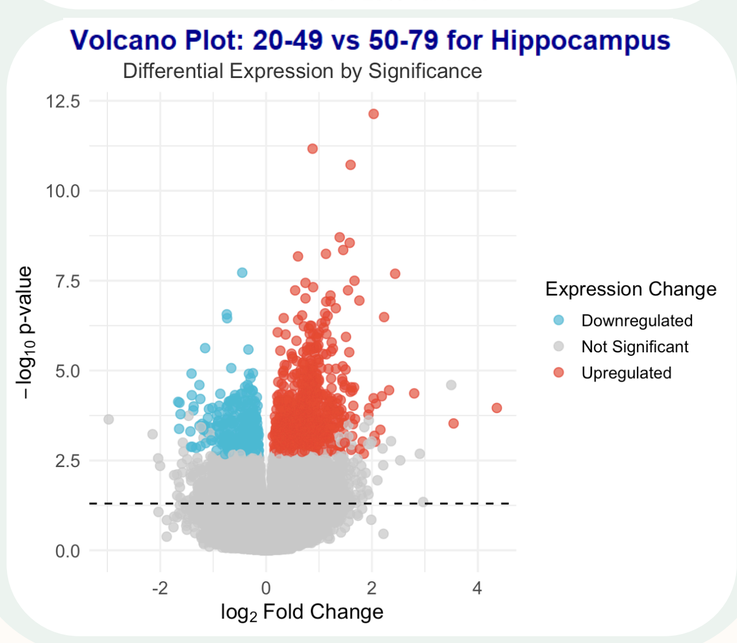
- The hippocampus is **particularly vulnerable** to the aging process (Bettio et al., 2017).
- Hippocampal volume peaks in the fourth decade and **declines progressively with age** (Gohel et al., 2025).
- Brain aging involved expression of **genes** linked to **mitochondrial dysfunction**, **inflammation**, and **stress responses** (Zeier et al., 2011).

Are these declines visible in gene expression?

PCA: No clear clustering → after PERMANOVA: significant effect (p-value : 0.001***), 4.7% of variance explained by age.

Volcano plot: Comparing Young (20-49) vs. Old (50-79) shows significant up- (1572) and downregulated (753) genes.





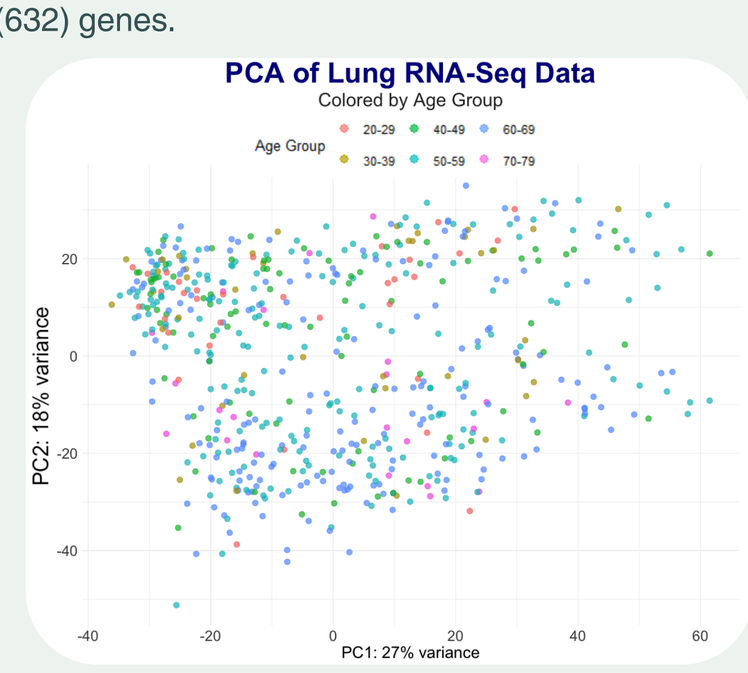
LUNG

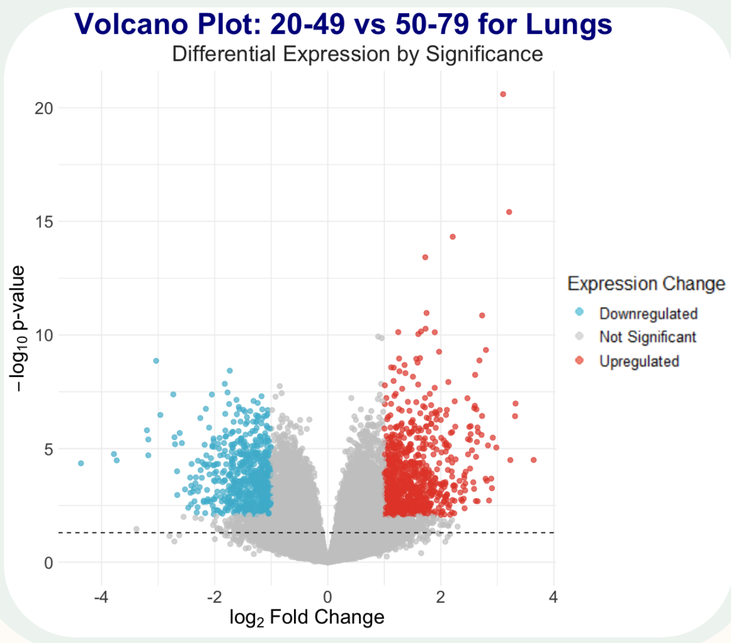
- Aging **impairs lung elasticity**, reduces immune defenses, and increases susceptibility to **respiratory diseases** like pneumonia and COPD (Berger et al., 2010)
- Some genes are more **up/downregulated in the lungs** when we have compared different age groups in **previous RNAseq research** (Jeong et al., 2020)

Are these declines visible in gene expression?

PCA: No clear age-group clustering → After PERMANOVA: Significant clustering, 23.83% of variance explained by age with p-value = 0.001

Volcano plot: Comparing Young (20–49) vs Old (50–79) shows significant up- (836) and downregulated (632) genes.





CONCLUSION

Gene expression changes with age are organ-specific:

- **Metabolic and stress response genes** upregulated and **structural and oxidative stress-related genes** downregulated in the **aorta**
- **Immune activation and RNA editing genes** upregulated and **neuronal structure genes** downregulated in the **hippocampus**
- **Tissue repair and inflammation genes** upregulated and **airway defense and regeneration** downregulated in the **lung**

Overall, very little overlap in age-related gene changes was observed across organs, with statistical analysis confirming no significant shared changes, highlighting that aging drives distinct molecular processes in different tissues.

REFERENCES

Transcriptomic Reprogramming in Senescence Induced Fibroblasts

Silke Rietvelt[1], Lars Huizinga[1], Yara Akaleya[1], Ammar Akaleya[1], Emircan Gülge[1], Rianne van Dekken[1]
[1] MSc Biomedical Sciences, University of Groningen

Introduction

- Senescent cells contribute to tumor suppression, tissue repair, development, and aging, but their persistence drives inflammation and tissue dysfunction via the senescence-associated secretory phenotype (SASP).
- Cellular senescence is an irreversible growth arrest induced by stressors such as ionizing radiation, involving DNA damage, p53–p21 signaling, and SASP activation.
- In contrast, quiescence is a reversible, non-damaging arrest occurring under normal conditions like nutrient deprivation.
- The Hernandez et al. RNA-seq dataset (proliferating, quiescent, and irradiated fibroblasts at days 4, 10, and 20) enables a time-resolved comparison of transcriptional changes in radiation-induced senescence versus quiescence.

Research Question

How does the transcriptomic profile of primary human foreskin fibroblasts change over time during ionizing-radiation-induced senescence (days 4, 10, and 20 post-irradiation) compared with quiescent and proliferating cells?

Hypotheses

Following ionizing radiation, fibroblasts are expected to show:

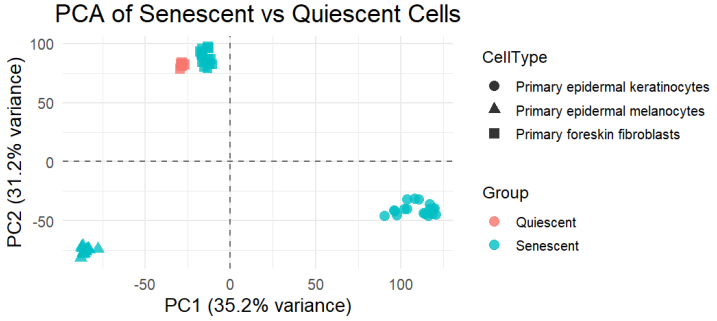
- DNA damage response and cell-cycle arrest at **day 4**
- peak SASP and inflammation at **day 10**
- stabilization of late senescence features, including ECM and chromatin remodeling, by **day 20**.

Material and Methods



Results

Figure 1: Principal Component Analysis (PCA) of quiescent and senescent cells across multiple cell types shows that quiescent cells are only present in primary foreskin fibroblasts.



Results

Figure 2: Volcano plot of differential gene expression between IR day 20 and quiescent fibroblasts, with significant upregulation of senescence- and DNA damage–related genes and downregulation of cell-cycle genes.

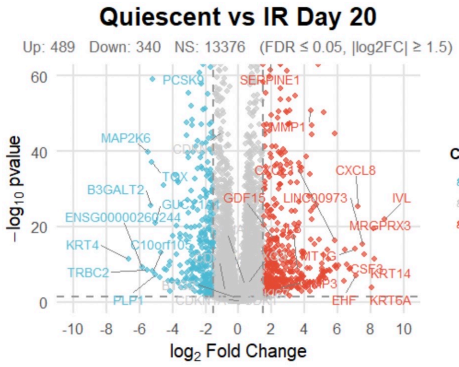
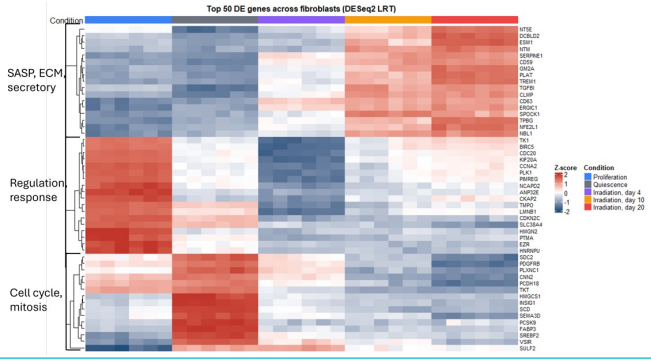


Figure 3: Heatmap of the top 50 differentially expressed genes across fibroblast conditions reveals progressive transcriptional reprogramming during irradiation-induced senescence.



Conclusion

- Quiescent cells were identified only in fibroblasts (Fig. 1), establishing them as the focus of our analyses.
- Transcriptomic data showed downregulation of cell-cycle genes and upregulation of DNA-damage and senescence pathways in quiescent fibroblasts (Fig. 2).
- Fibroblasts exhibited progressive transcriptional reprogramming from early DNA-damage response (day 4) to SASP activation and ECM remodeling (days 10–20) (Fig. 3).
- Classification effectively distinguished proliferating, quiescent, and senescent states, capturing the temporal dynamics of radiation-induced senescence.
- Together, these findings support fibroblasts as a robust model system for studying senescence at the transcriptomic level.

Future Perspective

- Extend analyses to other cell types and stressors to test fibroblast specificity.
- Apply trajectory and machine-learning models to capture transitions between cell states.
- Integrate single-cell and multi-omics data to uncover heterogeneity within senescent populations

References and R-codes can be observed through the QR code.

COPD: FROM BAD TO WORSE

DIFFERENTIAL GENE EXPRESSION IN COPD PROGRESSION

Elena Ascension, Erwin Feringa, Vera Horneman, Wendy Lutjeboer, Leanne Speelman & Dian van Zanten

university of groningen

RESEARCH QUESTION: What gene expression differences distinguish moderate COPD from mild COPD, what are their biological functions and could they be used as progression markers?

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a persistent lung condition caused by damage to the lungs. The damage leads to **swelling and inflammation in the airways**, restricting the flow of air into and out of the lungs. COPD is usually caused by long-term exposure to cigarette smoke, dust, or chemicals [1]. This case study examines the difference in gene expression between mild and moderate COPD, using the dataset of Kim et al (2015). **Mild COPD** is characterized by mild airway obstruction, while **moderate COPD** is characterized with lung damage and functional decline [2].

METHODS

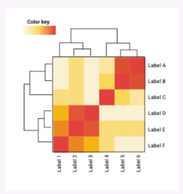


DGE Analysis selecting stage 1 and 2 COPD in R with the dataset from Kim et al. (2015).

16 significant differentially expressed genes with an FDR ≤0.01 were found.

5 upregulated genes

11 downregulated genes



Made with Biorender.

HEATMAP



Figure 3: **Heatmap** showing gene expression differences between normal (green), mild (blue) and moderate (red) COPD. The figure above shows a heat map in which the y-axis displays a list of the 16 most significant genes with the different gene expression between mild and moderate COPD. In addition, a color scale is visible based on the z-score. On the right-hand side of the heat map showing high gene expressing (+1) in pink and low gene expression (-1) in blue. Two genes, which showed significant expressing on the vulcano and MA plot are underlined in red.

DGE VISUALISATION

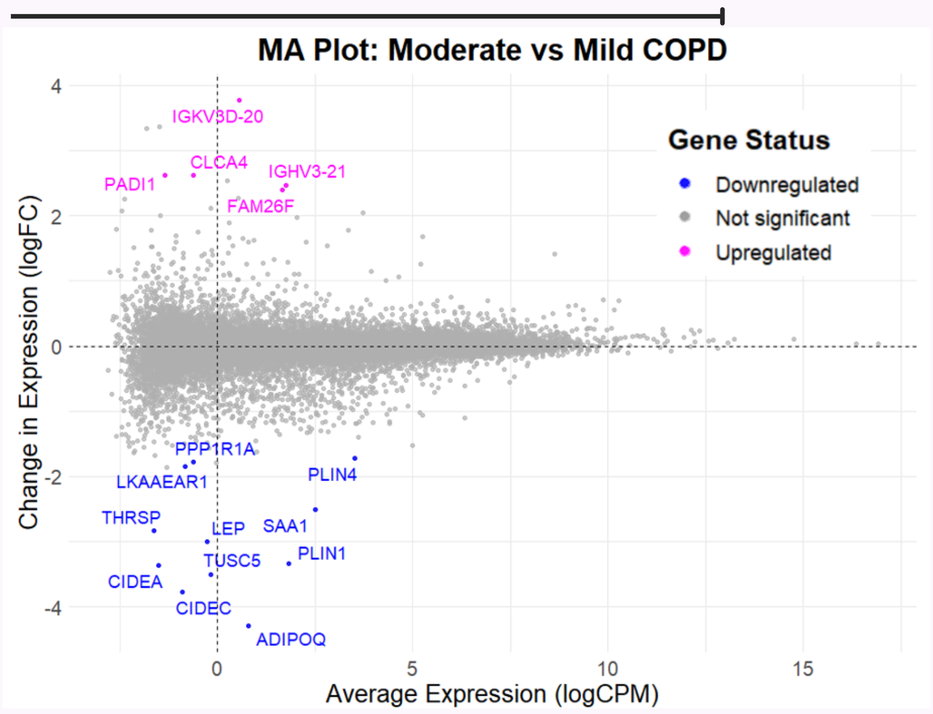


Figure 1: **MA plot** showing the change in gene expression for stage 2 COPD compared to stage 1 COPD on the y-axis against the average expression on the x-axis. Significantly up- and downregulated genes are highlighted in magenta and blue respectively. The vertical dashed line shows an average gene expression of 1 Count Per Million.

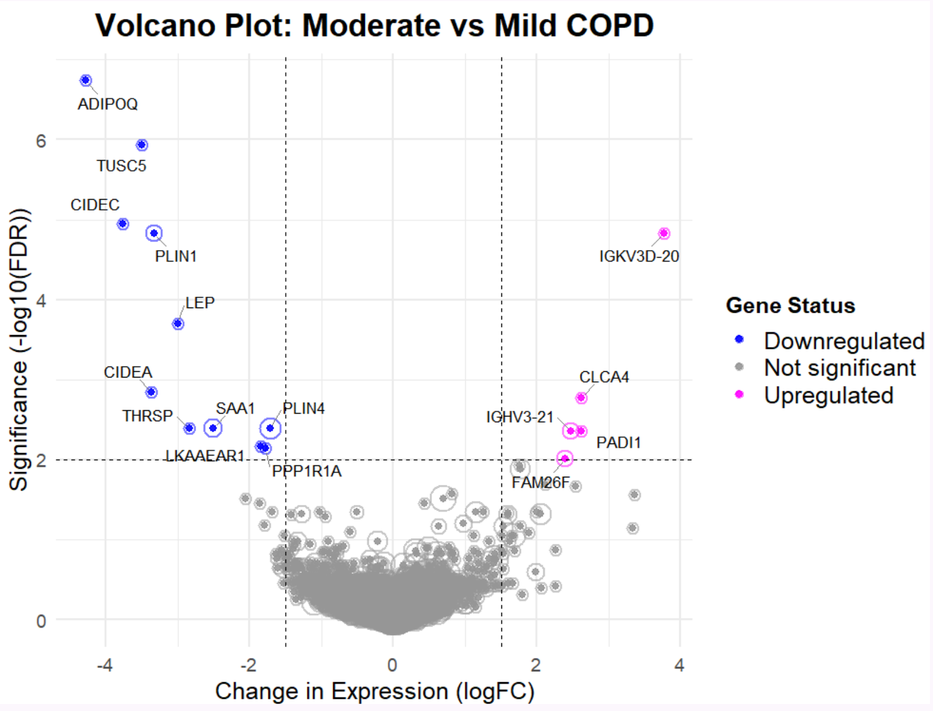


***Figure* 2: Volcano Plot** showing the magnitude of fold change on the x-axis and the significance of the differences on the y-axis. The general expression of the genes is highlighted by the sphere surrounding the data points. The genes above the horizontal axis are significantly up- or down regulated between moderate compared to mild COPD. The genes inside the dotted lines show relatively low expressional differences between these two stages of the disease.

IGKV3D-20 (upregulated) and **ADIPOQ** (downregulated):

- Largest Fold Changes
- Highest significance
- Above threshold average gene expression of 1 CPM.

DIFFERENCES IN BIOLOGICAL FUNCTION

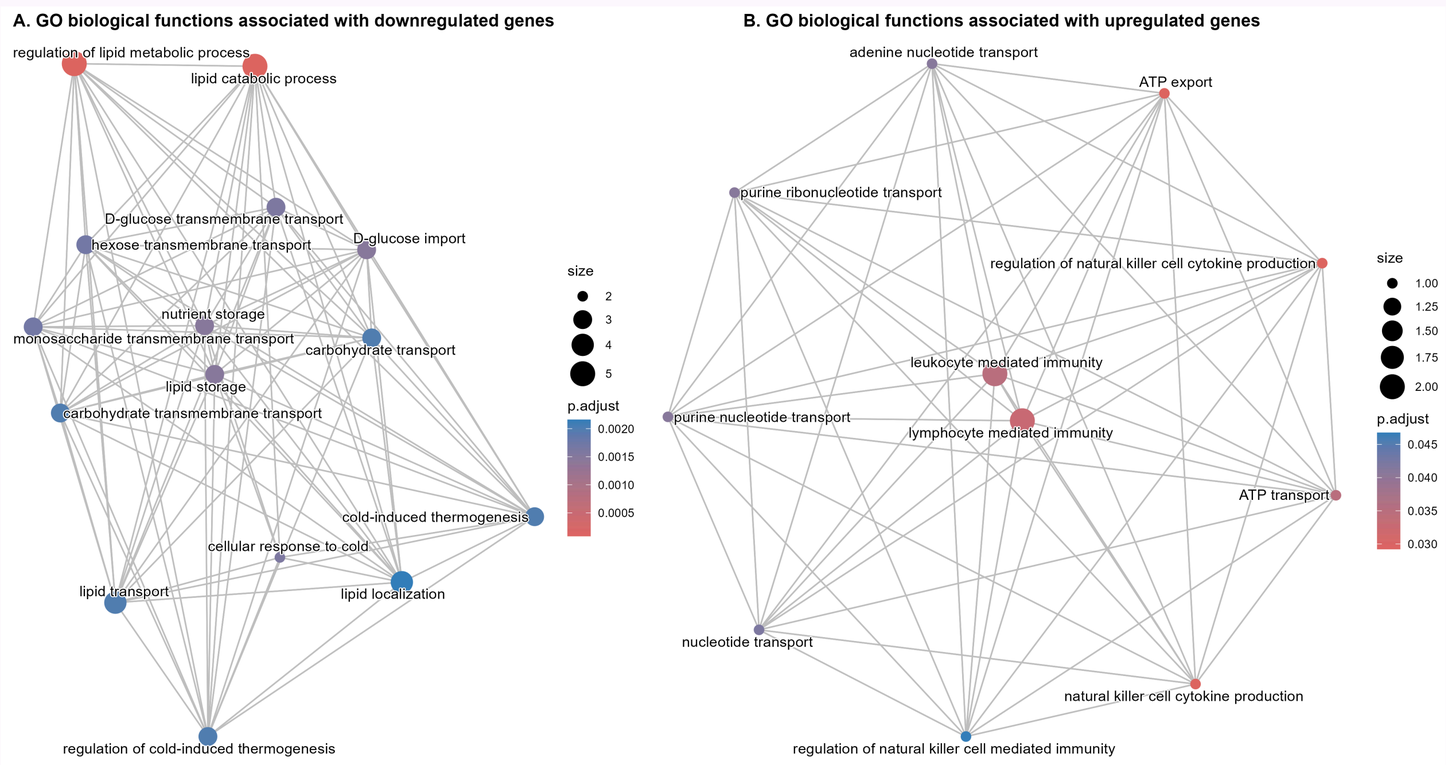


Figure 4: **Gene ontology term enrichment analysis** performed on the A: 11 found significantly downregulated genes and B: 5 significantly upregulated genes between moderate compared to mild COPD patients. The sizing showcases the number of genes associated with the biological process. Graph A showcases downregulated regulation of lipid metabolic processes, lipid catabolic processes amongst other metabolic processes while graph B shows upregulation within immunological pathways.

CONCLUSION

- **16** differentially expressed genes were found
  - **5** were **upregulated** in moderate COPD
  - **11** were **downregulated** in moderate COPD
  - Most interesting genes → **IGKV3D** and **ADIPOQ**
- Important functions of genes
  - **Immune response** upregulated
  - **Lipid metabolism** downregulated
- High **inter-patient variability**
  - No progression markers

FUTURE PERSPECTIVES

- Single cell RNA sequencing
- Study all COPD stages (incl. stage 3 (severe) COPD)
- Larger sample size

REFERENCES AND SUPPLEMENTARY DATA